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Vol. 1. 1913. No. 7.

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TROPICAL DISEASES BUREAU.

TROPICAL DISEASES BULLETIN.

Vol. I.] 1913. [No. 7.

KALA AZAR.

Indian Kala Azar.

Eightieth Annual Meeting of the British Medical Association. Held in Liverpool, July 19th-26th, 1912. Section of Tropical Medicine —Papers dealing with Leishmaniasis.—*Brit. Med. Jl.* 1912. Nov. 2. pp. 1194-1199.

1. In a paper entitled "The Kala Azar Problem" Patton emphasises many of the points which have been more fully discussed by him in a publication already reviewed. (See this *Bulletin* No. 1, pp. 1-3.)

2. "Some Experimental Facts re Kala Azar (Indian)" is the title of a paper by Row, which is a preliminary note to the papers by the same author reviewed below.

3. In a paper on "Some Insect Flagellates and the Problem of the Transmission of Leishmania" Fantham points out how the occurrence of natural flagellates in the gut of various insects which have been supposed to be possible transmitters of leishmania may give rise to errors in experimental work. *Pulex irritans* has been shown by Porter to harbour *Crithidia pulicis*, *Ctenocephalus canis* harbours a herpetomonas for which the writer proposes the name *Herpetomonas ctenocephali*, and Patton has recorded a herpetomonas in *Ctenocephalus felis*. The author has recorded *Herpetomonas pediculi* from *Pediculus vestimenti* and has found a similar flagellate in *Pediculus capitis*. In mosquitoes *Herpetomonas culicis* was recorded by Novy, Patton and others from *Culex pipiens* and *Culex fatigans* both in the larval and adult stages. *Crithidia fasciculata* (Leger) occurs in various species of Anopheles and Wenyon has recorded a Herpetomonas from the larva of *Stegomyia fasciata*. Phlebotomus, which has been suspected to be a transmitter of oriental sore, was shown by Wenyon to harbour a natural herpetomonas, while house flies are commonly infected with *Herpetomonas muscae domesticae*. All these flagellates pass through leishmania-like stages and confusion of these with true leishmania can readily arise. The well known fact that bed bugs have never yet been shown to harbour a natural flagellate is emphasised.

(28291—2.) Wt. P 2690—71. 2000. 2/13. D & S.

In the discussion on the subject of leishmaniasis H. SEIDELIN mentioned the occurrence of dermal leishmaniasis in Yucatan (see this *Bulletin* No. 1, p. 13). MADDEN made some remarks on specimens of leishmania which he was demonstrating from a disease in Egypt, which he had been accustomed to call papilliferous degeneration of the skin. The disease was fully described by FERGUSON and RICHARDS, who discovered *Leishmania tropica* in the lesions, in a paper in the *Annals of Tropical Medicine & Parasitology*, 1910. July, Vol. 4. No. 2, under the name of parasitic granuloma (see *Kala Azar Bulletin* No. 1, p. 60). BALFOUR stated that he had examined a considerable number of bed bugs (*Cimex lectularius*) in Khartoum without finding any evidence of flagellate infection. He pointed out the danger of confusing mere cultural changes in the insect's intestine with a true developmental cycle and finally referred to the observation made by ARCHIBALD that the dark field method demonstrated that granule shedding occurred in the flagellate cultural forms of *Leishmania tropica* and that in this fact there might lie hidden the solution of the problem of transmission of leishmaniasis.

BAYON gave a demonstration of specimens relating to the transmission of artificial cultures of *Leishmania infantum* to rats and mice. He had failed to produce a general infection in these animals by intraperitoneal injection of the cultures and was able to confirm the observation of DELANOË and VISENTINI that the parasites were taken up and destroyed by the mononuclear cells. A culture was obtained from the peritoneal fluid of one mouse killed four hours after injection.

C. M. Wenyon.

Row (R.). **Some Experimental Facts *re* Kala Azar (Indian).**—*Jl. Trop. Med. & Hyg.* 1912. Nov. 1. Vol. 15. No. 21. pp. 327-328; and 1913. Jan. 1. Vol. 16. No. 1. pp. 1-2.

These two papers contain accounts of experiments on the production of local lesions in animals with the virus of Indian kala azar. In the first place two monkeys (*Macacus sinicus*) were inoculated on each side of the forehead, one by rubbing virus from a human spleen, containing *Leishmania donovani*, into the scarified skin, and the other by injecting subcutaneously (0·3 cc. on one side and 0·15 cc. on the other) liquid from a fifth subculture on NNN medium of the leishmania from the same spleen. In the first monkey inoculated with the virus direct from the spleen on March 16, a small nodule had developed on the left side by May 22nd and by June 6th two similar nodules had developed on the right side. In all of these leishmania were found and material from one of the nodules produced a similar nodule when inoculated into another monkey. These nodules were histologically of the nature of young fibromata which ultimately absorbed leading to no generalised infection. The monkey inoculated from the culture of the leishmania on February 2nd was found to have developed a nodule on each side of the forehead at the site of inoculation on July 2nd. The nodules were freely movable under the skin and contained leishmania. One of the nodules was

excised a fortnight after its appearance and half of it was ground up with 1 c.cm. of ·6 per cent. saline solution. The remaining nodule increased in size for two months, then began to dwindle, and finally disappeared about four months after its first appearance. The monkey remained quite well and showed no sign of general infection. The saline emulsion obtained from the crushed nodule was injected intraperitoneally into two mice and one *Macacus sinicus*. All these animals developed generalised leishmaniasis with numbers of leishmania in the internal organs. One other mouse injected with some of the juice expressed from the nodule also developed a general infection. The material obtained from the organs of the mice was injected intraperitoneally into six other mice; these however did not become infected, though the material injected contained many more parasites than that obtained originally by crushing the excised nodule from the monkey. The infected monkey was found to have parasites in its liver five months after injection, while the mice became generally infected in about six weeks. It appears that the virus loses its virulence for mice on passing through mice. The production of a local lesion by the injection of *L. donovani* or its culture, and the further production of a general infection in animals by injection of parasites from the local lesion, is of the utmost interest from the point of view of the relation of the two diseases, oriental sore and kala azar. The nodules which developed at the site of inoculation were rather of the nature of fibromata than the papules characteristic of oriental sore. In this connection it is of interest to remember that VOLPINO produced a local lesion containing leishmania in the cornea of a rabbit, by scarification and application of material from the spleen of a dog infected with kala azar (see *Kala Azar Bulletin* No. 1, p. 7).

C. M. W.

MEDITERRANEAN KALA AZAR.

LAVERAN (A.). **Infections des Souris et des Rats dues au Kala-Azar Méditérranéen et au Kala-Azar Indien.**—*Bull. Soc. Path. Exot.* 1912. Nov. Vol. 5. No. 9. pp. 715-721.

In this paper the author records experiments conducted with the virus of Tunisian kala azar. In an earlier paper he has shown that a general infection can be produced in mice by intraperitoneal injection of material from the spleen of infected dogs. Similarly W. L. and N. K. YAKIMOFF have infected mice by injecting cultures intravenously into the caudal vein and also by intraperitoneal injection of virus from an infected animal. The author now reports that in 26 mice injected intraperitoneally with material from the spleen, liver, or bone marrow of infected dogs or mice the following results were noted.—There was a general infection heavy in four, moderate in four, and slight in thirteen, while five showed parasites only in the peritoneal exudate which results from the inoculation. Two of these mice with general infection were heavily infected when killed, 24 and 31 days after inoculation; one was heavily infected when killed 138 days after inoculation, but the author remarks that the long duration of the infection is exceptional; other mice killed, from 127 to 203 days

after inoculation, showed only a scanty infection. One mouse died with a general infection, but though no other cause than the leishmania infection could be found to account for its death the author hesitates to attribute it to this, since other mice much more heavily infected recovered.

Infection is best produced by the intraperitoneal injection of material from infected organs of another animal. Parasites can be recovered from the peritoneal exudate after eight days. They are included in mononuclear cells as a rule, but are sometimes free. Attention is called to the fact that intraperitoneal injection of cultures does not produce an infection owing to the fact that the flagellate forms are quickly ingested and destroyed by the leucocytes. Once a slight infection was produced by injecting a culture into the liver of a mouse.

The author hoped that when once a general infection had been produced in mice it would be possible to increase the virulence of the leishmania for mice by subinoculations. The contrary has proved to be the case, for the strain tends to lose its virulence in the subinoculations in mice, just as the author has found to be the case with dogs.

Enlargement of the spleen is a constant feature of infection. Of 24 mice infected, in five the spleen was very large (five to six times its normal volume which is usually 7-8 cg. for a mouse of 20 g.), in ten it was three to four times its normal volume, while in nine it was one and a half to two and a half times the normal. In one mouse the weight of the spleen was 45 cg. while in several it was 25-30 cg. Parasites were found nineteen times in the spleen, ten times in the liver and five times in the bone marrow. The spleen is thus most usually infected.

A rat inoculated intraperitoneally with virus from an infected animal died twelve days later from diarrhoea. It was found to have numerous leishmania in the peritoneal exudate and a scanty infection of the spleen which was hypertrophied. W. L. and N. K. Yakimoff have recorded the infection of a rat but in their case the parasites were only recovered by culture on NNN medium.

In discussing his results the author records a communication he has received from Row on the subject of his inoculations of *Leishmania donovani* (see Row's paper above). Patton's successful inoculation of a rat with the Indian kala azar virus is mentioned and though the Indian virus appears to be more virulent for these animals than the Mediterranean the author sees in these results an indication of the identity of the Eastern and Western diseases.

C. M. W.

Visentini (Arrigo). **On the Morphology of the Leishmania of Italian Kala Azar. Third Communication: Cytological Researches on Leishmania in Cultures.**—*Quart. Jl. Micros. Sci.* 1912. Dec. Vol. 58. No. 2. (New Series No. 230.) pp. 353-371. With 2 plates.

The paper describes the flagellate forms of leishmania when these are fixed and prepared by methods more rational than smearing and drying in films. The medium used for culture was the well known NNN medium prepared in the usual way.

The method of abstracting the blood from the rabbit is one which has given good quantities, an important matter from the point of view of economy. The anaesthetised animal is fixed on its back with the throat exposed. After shaving and sterilising the skin, the trachea is laid bare by a median incision, the carotid is isolated from the nerves and tied as near the skull as possible. The thyroid artery is isolated and tied near the carotid in order that it may serve as a handle for holding the carotid in position. A sterile flask containing beads is held near the wound, the carotid is divided near the cranial ligature and by means of forceps holding the thyroid artery the jet of blood is directed into the flask. In this way as much as 55-60 cc. of blood can be collected and if the carotid is quickly tied and the wound sutured the animal may recover.

As regards the structure of the flagellates in these cultures it is found that the trophonucleus is of the vesicular type. There is a nuclear membrane enclosing a clear space at the centre of which is a karyosome, within which a small granule, the centriole, may sometimes be distinguished. The karyosome is sometimes seen to be connected with the nuclear membrane by fine radiating threads and very fine granules may occur on the inner surface of the nuclear membrane. The kinetonucleus is described as having essentially the same structure, with the exception that the karyosome is transversely elongated. At the anterior part of the clear area surrounding the kinetonuclear karyosome is the basal granule from which the rhizoplast of the flagellum springs. In other cases the author describes the flagellar rhizoplast as uniting directly with the karyosome, in which case it is assumed that the basal granule is within the karyosome as the centriole was within the karyosome of the trophonucleus. In nuclear division the centriole divides and with it the karyosome. The two halves of the centriole may remain connected for some time by a centrodesmose. The nuclear membrane persists during this division. The author speaks of the splitting of the flagellum into two, one of full length and the other shorter. Later the shorter one approximates in length to the other. [The figures however do not show this splitting and are rather illustrations of the view that the new flagellum is an entirely new formation formed as an outgrowth of the divided basal granule. This paper is a confirmation in nearly every detail of the description given previously by Wenyon of the structure of the cultural forms of *Leishmania tropica* from Bagdad.]

C. M. W.

Spagnolio (G.) **Leishmaniosi Interna (Kala Azar) a Messina.—Nuovi Esempi Clinici e Sguardo Riassuntivo.** [Leishmaniasis (Kala Azar) in Messina. A Resumé of the Clinical Features of some New Cases].—*Malaria e Malat. d. Paesi Caldi.* 1912. Nov. Vol. 3. No. 11. pp. 307-310.

It is pointed out that the view expressed by Feletti and Gabbi that kala azar was a widespread disease in Sicily is amply justified. Jemma has in little more than two years diagnosed by spleen puncture 66 cases, Longo 45 cases, and Feletti, Pulvirenti, Licciardi a still greater number. During this year the

author himself has definitely diagnosed a further fifteen cases in all of which leishmania were discovered. A short review of each of these cases is given.

In the majority of cases it is stated that dogs were not kept in the houses from which they came. In two a culture of the leishmania was obtained by ROGERS' method in citrated blood. In one instance it was found that the mother of the child had died shortly before from a malady which the author feels sure was kala azar. If this be so it is another instance of the disease occurring in an adult.

C. M. W.

DI CRISTINA (G.). **I Corpi di Leishman nell 'Organismo infetto vanno incontro a Processi Litici? (Nota Preventiva.)** [Disappearance of Leishman's Bodies from an Infected Organ after Death.]—*Pathologica.* 1912. Nov. 1. Vol. 4. No. 96. pp. 643-645.

The author describes a case of infantile kala azar in a child of ten months. Numerous parasites were discovered by spleen puncture. About fifteen days later the child died and, though an autopsy was performed two hours after death, no typical leishmania were to be found in smears of the spleen, liver, or bone marrow, stained by Leishman's modification of the Romanowsky stain. In sections of the liver, however, a few cells containing parasites were made out. The author believes that the parasites were destroyed shortly before death owing to the appearance in the blood of some anti-leishmania substance. A somewhat similar case in which numerous leishmania were found in the spleen before death and none after was noted by LIGNOS (see this *Bulletin* No. 1, p. 4).

C. M. W.

LONGO (A.). **Tentativi Immunodiagnostici ed Immunoterapeutici nella Leishmaniosi Infantile.** [Attempts at Serum Diagnosis and Immunisation in Infantile Leishmaniasis.]—*Policlinico.* Sez. medica. 1912. Oct. Vol. 19. No. 10. pp. 446-452.

In these investigations the blood of three children, in what the author calls the second stage of kala azar, was used. As controls he employed the blood of a healthy adult, a child suffering from infantile paralysis and another from vulvo-vaginitis. The agglutinating power of the blood in various dilutions was tested against cultures of leishmania. None of the cases showed any agglutination power. LEVADITI and MUTERMILCH showed that the serum of guinea-pigs infected with various trypanosomes, when mixed with trypanosomes and leucocytes from either a healthy or infected guinea-pig, caused the leucocytes to attack and eventually ingest the trypanosomes. Tested with cultures of leishmania the serum of the kala azar cases had no such action. No evidence could be obtained that either precipitins or specific amboceptors existed in the blood of the kala azar cases. Two cases were treated with injections of killed cultures, but this was not attended with any good result, nor did antibodies appear in the blood.

C. M. W.

CARONIA (G.). **Tentativi d'Immunizzazione attiva per la Leishmaniosi Umana nel Bambino Sano.** [Attempts at Active Immunisation in the Healthy Child by Human Leishmaniasis.]—*Pathologica.* 1912. Dec. 1. Vol. 4. No. 98. pp. 724-725.

This paper appears to be a further illustration of results obtained by the author in co-operation with di CRISTINA (see this *Bulletin* No. 1, p. 7). In the present instance, a healthy child two years of age, whose blood did not agglutinate cultural forms of leishmania and gave a negative reaction to complement deviation, was injected daily for five days with 1 cc. of inactivated culture of leishmania. The reactions were again tested, with negative result, while the condition of the blood cells remained unchanged. The treatment was repeated for a further six days after which both in the case of agglutination and complement deviation a positive result was obtained. The leishmania thus agree with other pathogenic organisms in stimulating the production of antibodies.

C. M. W.

MASSAGLIA (A.). **Contributo allo Studio delle Infezioni da *Leishmania infantum.* Nota Preventiva.** [A Study of the Infection due to *Leishmania infantum.*]—*Pathologica.* 1912. June 1. Vol. 4. No. 86. pp. 308-310.

A dog was inoculated from a case of kala azar in a child on December 7th, 1907. After the virus had passed through two dogs a bitch was inoculated on July 20th, 1909. It was found by NICOLLE in June 1910 to be infected. Two small dogs (age about three months) were placed in the kennel with this dog, which was subjected to splenectomy on July 29th, 1910. The dog recovered from the operation and lived with the two small dogs until May 1911, when all three were killed, and were found to be uninfected, though the spleen of the oldest dog was infected when removed at the operation.

C. M. W.

CANNATA (S.). **Quarta Serie di Ricerche Ematologiche nell' Anemia da Leishmania.** [Fourth Series of Haematological Researches on Leishmanial Anaemia.]—*La Pediatria.* 1912. No. 8.

In this paper the author gives an account of blood examinations made on 24 cases of infantile kala azar, which, with the cases previously examined by him (*Kala Azar Bulletin* No. 2, p. 81), bring the total up to 56. As was reported in his earlier papers the author still finds that blood examinations in this disease cannot be considered of absolute importance as an aid to diagnosis. Of the 56 cases 58·9 per cent. showed leucopenia, in 30·4 per cent. the leucocytes were normal in number or only slightly reduced, while in 10·7 per cent. there was a leucocytosis. Of the leucocytes the lymphocytes were most numerous. In this paper as in the earlier ones a table is given showing the results of the blood examinations.

C. M. W.

SPAGNOLIO (G.). **Sulla Coltivabilità della Leishmania, così detta Infantum, nel Sangue Splenico Citratato o Mezzo di Rogers.** [On the Cultivability of the so-called *Leishmania infantum* in Citrated Splenic Blood after the Method of Rogers.]—*Malaria e Malat. d. Paesi Caldi.* 1913. Vol. 4. No. 1. pp. 2-7.

Owing to the fact that the possibility of cultivating the parasite of Mediterranean kala azar after ROGERS' original method has been disputed by some observers the author has again undertaken to settle this question. He points out that the parasite of Indian kala azar does not always develop into flagellates in citrate solution and this is probably also true of the Mediterranean form. Culture was attempted in six cases. In two cases in which the product from spleen puncture was added to ten per cent. citrate solution and incubated at 30° C. a negative result was obtained. In another case ten per cent. citrate solution in ·75 per cent. sodium chloride solution was used, also with a negative result, while the employment of a two per cent. citrate in ·5 per cent. sodium chloride solution showed flagellates in 48 hours. In the fourth and fifth cases also the latter solution gave a positive result. In the sixth case the blood from the spleen was drawn up into the syringe containing half a cubic centimeter of ten per cent. sodium citrate solution. Part of the mixture in the syringe was then added to 3 cc. of a two per cent. citrate solution in ·8 per cent. saline, contained in a test tube. The tube and syringe were incubated at 30° C. After 48 hours flagellates had developed both in the tube and in the syringe. These experiments clearly establish the claim of JEMMA and LONGO to have observed the development of flagellates in citrate solution, to which leishmania from infected spleens of children, suffering from infantile kala azar, had been added, and show that as regards culture the parasites of the Mediterranean and Indian diseases do not differ from one another.

C. M. W.

SCORDO (Fr.). **I Leucociti della Cavia e del Coniglio in contatto delle Forme Flagellate della *Leishmania Donovani* "in vitro" e nel Corpo degli Animali.** [Leucocytes of the Guinea Pig and Rabbit in contact with the Flagellate Forms of *Leishmania donovani* in vitro and in the Animal Body.]—*Malaria e Malat. d. Paesi Caldi.* 1912. Sept.-Oct. Vol. 3. Nos. 9-10. pp. 246-249. With 1 plate.

This paper is a record of experiments on the behaviour of cultural forms of leishmania when left in contact with leucocytes obtained from artificially produced exudate from the pleura of guinea pigs or the peritoneum of rabbits. VISENTINI (see this *Bulletin* No. 1, p. 9) has shown that the flagellate forms are quickly ingested and destroyed by the leucocytes in the peritoneal cavity of guinea pigs. The author of this paper has obtained similar results but he has found that when left in contact with leucocytes *in vitro* instead of in the peritoneal cavity, digestion

does not proceed so rapidly. Ingested forms are still recognisable after a period of 24 hours, whereas two hours is sufficient for their destruction by the leucocytes when in the peritoneal cavity.

C. M. W.

NICOLLE (C.) & BLAIZOT (L.). **Virulence des Cultures de** *Leishmania infantum.* **Sensibilité du Chacal au Virus du Kala Azar Tunisien.** *Bull. Soc. Path. Exot.* 1912. Nov. Vol. 5. No. 9. pp. 721-723.

Four young rabbits and four young guinea pigs were inoculated intravenously with cultures of leishmania from a case of infantile kala azar. Two young dogs and a kitten were similarly inoculated, and one dog intraperitoneally. Of all these animals only one of the young dogs intravenously inoculated became infected. The animal was killed on the 72nd day and from its organs another dog and two jackals were inoculated intraperitoneally. The dog and one of the jackals became infected. The jackal was apparently in good condition but was found infected when killed on the 84th day of experiment. The parasites were most numerous in its bone marrow but the liver and spleen were also infected.

C. M. W.

GABBI (U.). (i.) **Sulla Identità delle** *Leishmanie infantum* **e** *Donovani.* (ii.) **Il Kala-Azar infantile e la** *Leishmania infantum* **al Lume delle Ultime Ricerche.** [On the Identity of *Leishmania infantum* and *L. donovani.*]—*Malaria e Malat. d. Paesi Caldi.* 1912. Dec. Vol. 3. No. 12. pp. 334-335 and 336-347.

The two papers here reviewed occupy ten pages. They consist of a summary of recent work on kala azar with a view to proving the identity of the various forms of the disease met with in different parts of the world. The author is convinced that the kala azar of India, the Mediterranean, the Sudan, China and other countries is always the same disease and that *Leishmania infantum* as the name of a distinct species lapses in favour of *Leishmania donovani.*

C. M. W.

MARZINOWSKY (E. I.). **Maladies Voisines de la Malaria en Russie, Kala-azar, Fièvre de Malte, etc.**—*Bull. Soc. Path. Exot.* 1912. Dec. Vol. 5. No. 10. pp. 868-875.

It is pointed out that in the south and south-east of Russia a febrile form of splenomegaly exists, in which malarial parasites cannot be found. These cases are probably kala azar and the author mentions the cases of this disease already described from Russia. The first was described by himself, the second by NIKAFOROFF, the third by KALATCHNIKOFF and the fourth by PETRONE. Four further unpublished cases were seen by GOURKO in Tiflis. To these must be added the case described by SLUKA and LARFLE from Taschkent. Details of the author's case are given and he draws attention to the occurrence of canine leishmaniasis in Transcaucasia as demonstrated by DJOUNKOWSKY (*Kala Azar Bulletin* No. 1, p. 16).

C. M. W.

TRANSMISSION.

WENYON (C. M.). **Experiments on the Behaviour of Leishmania and Allied Flagellates in Bugs and Fleas, with some Remarks on Previous Work.**—*Jl. London School Trop. Med.* 1912. Dec. Vol. 2. Part 1. pp. 13-26.

The first part of this paper contains a criticism of the view of PATTON that the bed bug is the true host of leishmania. It is pointed out that many organisms survive for a considerable time in the gut of the bug. The spirochaete of relapsing fever may be found three weeks after ingestion; *Schizotrypanum cruzi* will develop in the bug and be still infective to small animals after ten days; *Trypanosoma lewisi* will develop in the bug and on the eleventh day after ingestion crithidial, herpetomonad, and leishmanial forms can be found; and *Trypanosoma rhodesiense* persists for seven days or longer. This being the case it is not to be wondered at that the easily cultured leishmania will survive and develop in this insect. It is pointed out that the production of flagellate forms of leishmania in the gut of the bug and the subsequent transformation of these into round post-flagellate forms, as described by PATTON, is a further illustration of the similarity of the changes undergone by the leishmania in the gut of the bug and in the culture tube; for in old cultures similar round forms are produced. The extent of infection of the bug's gut with flagellate forms depends on the number of leishmania ingested. It is argued that if the bug were the true host then the ingestion of only a few leishmania should lead ultimately to a complete infection of the gut. Further the discovery of PATTON that a second feed of blood destroys those flagellates already developed in the gut is regarded as an additional argument against the bug hypothesis, for in the case of *Trypanosoma lewisi* and *Herpetomonas* in their true host, the flea, repeated feeds of blood have no effect in reducing the infection. The author obtained some evidence that *Leishmania tropica* would develop to flagellate forms in the gut of *Stegomyia fasciata* in Bagdad. Patton concluded that the forms seen by the author in the mosquito were probably flagellates peculiar to the mosquito. It is pointed out in this paper that it was proved that the mosquitoes to the extent of ten per cent. took up leishmania when fed upon an oriental sore, and that flagellates were found in practically the same percentage when the mosquitoes were dissected at suitable intervals after feeding on the sore; on the other hand no flagellates were found in the same number of controls dissected after similar intervals after feeding upon a healthy person. This being the case, it is claimed that it is more reasonable to assume that the flagellates were developed from the leishmania than that they were peculiar to the mosquitoes. On the question of nomenclature it is pointed out that the name *Herpetomonas* is applied to flagellates peculiar to insects, while the fact that the leishmania lives and produces disease in man and animals is proof that it is fundamentally different and justifies its inclusion in a separate genus, *Leishmania*.

Experiments with the object of infecting *Cimex lectularius* with *Leishmania tropica* were undertaken. These were carried out by feeding 105 bugs (all hatched in the laboratory except 18) on a non-ulcerating oriental sore in which leishmania were numerous. The following dissections were made:—

Number of bugs fed.	Number of days between feeding and dissection.	Number of bugs giving positive results.
26	9	0
14	8	0
29	7	0
10	6	0
12	4-6	0
5	3	1
9	2	2
Total 105		3

The three bugs giving a positive result were all hatched from the egg in the laboratory and had their first feed upon the sore. All bugs were incubated at 22°-23° C. The number of flagellates in the three bugs was small and none of the bugs dissected after longer intervals were infected, as they should have been if any active multiplication was taking place.

Attempts were also made to infect fleas, both *Pulex irritans* and *Ctenocephalus canis*, by feeding them upon the sore. For convenience the fleas were fixed in small loops of fine wire as Nöller has done in his *Trypanosoma lewisi* experiments (see *Sleeping Sickness Bulletin*, Vol. 4, No. 38, p. 215). While feeding, the flea repeatedly passes faeces which, at first consisting of digested blood mixed with fresh blood, soon become pure blood. It is easy to collect the faeces on cover glasses and, should the gut be infected with flagellates, some of these will be found in the stained films. By feeding the fleas upon uninfected individuals it can be determined whether the flea is infected or not prior to experiment. It was found that the faeces passed by the flea while it was feeding upon the sore contained *Leishmania tropica*, so that there was direct proof that the flea could take up the parasites from the sore. Fleas after feeding were kept in the incubator (22°-23° C.) for varying intervals (24 hours and upwards), when they were fed again and the faeces examined. If the leishmania were undergoing a development, some of these forms should appear in the faeces. In no case however was any trace of the leishmania taken up at one feed found at the next. These experiments involved about 50 feeds upon the sore. Some of the fleas (both human and dog) which had not become infected with leishmania after repeated feeds were readily infected with *Trypanosoma lewisi*, which underwent a complete development under the same conditions of experiment. No evidence was thus obtained that *Leishmania tropica* will develop either in the dog or human flea. It was further found that both the human and dog flea might be naturally infected with a *Herpetomonas* which in many of its stages was hardly

to be distinguished from developmental forms of leishmania. Accordingly the author doubts very much whether the flagellates described by BASILE, ALVAREZ and PEREIRA DA SILVA from fleas and supposed by them to be developmental forms of leishmania are in reality such.

A *Pulex irritans* infected with *Herpetomonas* was kept alive from August 24th to November 4th, during which time it had sixteen feeds of human blood and constantly passed large numbers of *Herpetomonas*, both flagellate and non-flagellate forms, in its faeces. A culture of the organism was obtained on NNN medium and it was shown that the small cystic forms passed in the faeces can withstand drying for at least 24 hours, for a culture on NNN medium was obtained by spreading the faeces on a cover glass, drying, and after 24 hours dropping the glass into the water of condensation in a culture tube of this medium.

C. M. W.

SERGENT (Edm. & Et.), L'HÉRITIER (A.), & LEMAIRE (G.). **Transmission de Leishmania de Chien à Chien par Piqûres de *Pulex serraticeps*.**—*Bull. Soc. Path. Exot.* 1912. Oct. Vol. 5. No. 8. pp. 595-597.

1. A young dog in good condition which had been in the Institute for two months was found to be free from leishmania as judged by a liver puncture. Between January 9th and 18th, and February 1st and 28th, it was bitten 82 times by fleas (*Ctenocephalus canis*) for periods of one to fifteen minutes. The fleas had been kept in tubes at 22° C. and they had been fed upon a dog infected with leishmania. The fleas were kept for eight days so that they were infected with a virus from one to eight days old. The dog was kept carefully free from all ectoparasites by constant washing with disinfectants. In March and April the dog lost flesh and showed the clinical signs of infection. The examination of the bone marrow always gave a negative result. In June the dog began to improve and on June 12th was killed. The liver gave a negative result both to culture and microscopic examination. Leishmania were however found in small numbers in the spleen and bone marrow, and a culture of flagellates was obtained on NNN medium from the spleen. No culture was obtained from the bone marrow. A control dog subjected to the same treatment save for the feeding of the fleas remained healthy and gave only negative results when killed on the same day as the experimental dog.

[This positive transmission experiment by the dog flea seems practically free from possible error. It is unfortunate that even when infected the liver gave a negative result both to microscopic examination and to culture, for it was by liver puncture performed before experiment that the dog was declared to be uninfected. Liver puncture is thus unreliable as a test of infection for experimental purposes.]

2. A single flea was fed every two days upon the infected dog. After a fortnight of this feeding it was fed daily for fifteen days upon a healthy dog. There was no evidence that the dog became infected and no leishmania were obtained either by culture or examination of smears.

3. A single flea was fed once upon an infected dog. Two days later it was fed upon a healthy dog and after that daily upon the same dog for fifteen days. No infection occurred.

As regards developmental forms in the fleas the authors found that two fleas which had fed upon the infected dog contained flagellates, while of nine fleas taken from presumably healthy dogs two were found infected. It has not been shown whether the flagellates are connected with the leishmania or not.

C. M. W.

BASILE (Carlo). **Sur l'Identité des Leishmanioses et sur leur Mode de Transmission.**—*Bull. Soc. Path. Exot.* 1912. Dec. Vol. 5. No. 10. pp. 812-816.

In this paper the author records a case of kala azar in a child aged four in the vicinity of Messina, where infection appears to have been acquired from a dog which was proved by microscopical examination of its bone marrow to have the disease. No other possible origin of the infection could be found. This case is regarded as a further demonstration of the transmission of kala azar from dog to child by means of the flea. The author reminds his readers that he proved beyond doubt in his transmission experiments that fleas are the carriers of the disease, and refers to the recent experiments of SERGENT, L'HÉRITIER and LEMAIRE.

The dog which was apparently the reservoir for the leishmania in this case was found to harbour fleas and ticks. Some of these were dissected and "protozoa, type leishmania" were discovered only in the fleas. The author admits that blood-sucking insects may harbour flagellates resembling leishmania, but claims that he ventured to describe flagellates from fleas only as such, when he had proved experimentally that the flea was the true host of leishmania.

Attention is drawn to the fact that the author was the first to record, in November 1910, the possibility of a spontaneous cure resulting in cases of infantile kala azar.

C. M. W.

FRANCHINI (G.). **Leishmania et Punaises.**—*Bull. Soc. Path. Exot.* 1912. Dec. Vol. 5. No. 10. pp. 817-819.

Experiments were conducted with the object of infecting bed bugs, *Cimex lectularius*, from cultures of *Leishmania infantum*. About 300 bugs, some of which were hatched in the laboratory, were starved and allowed to feed upon rich cultures. Only in six of these was any trace of the flagellates found. In two there were definite signs of degeneration, while in four the flagellates though not degenerating were quite unchanged and showed no sign of developing. The number of flagellates in each preparation was very small, so that in a comparatively short time the vast majority of those ingested had been destroyed. The author contrasts this result with that which he has had in his mosquito experiments, where large infections were found. He considers that the gut of *Cimex lectularius* is not suitable for the development of *Leishmania infantum*.

C. M. W.

FRANCHINI (G.). **Leishmanie e Zanzare. Ulteriori Esperienze con Zanzare o Parassiti Splenici.** [Leishmania and Mosquitoes.] —*Riforma Medica.* 1912. Dec. 7. Vol. 28. No. 49. pp. 1355-1358.

The outline of the results embodied in this paper was contained in an earlier note by the author which was reviewed in this *Bulletin* (No. 1, p. 9). The present communication contains little additional matter though the author now gives figures of the developmental forms of the leishmania in the mosquitoes. Some of these show flagellates which may very well be cultural forms of leishmania, while others show structures the nature of which it is impossible to decide. The author however believes that they have some connection with the development of the leishmania.

C. M. W.

VISENTINI (Arrigo). **Transmission of Leishmaniasis by means of Cultures and the Mechanism of the Natural Immunity in Rats and Guinea Pigs.**—*Quart. Jl. Micros. Sci.* 1912. Dec. Vol. 58. No. 2. (New Series. No. 230.) pp. 373-384. With 1 plate.

The author describes unsuccessful attempts to infect rats and guinea pigs by means of cultures of the leishmania of Mediterranean kala azar. He discusses the mechanism of immunity and shows that within the peritoneal cavity the cultural forms are quickly ingested and destroyed by mononuclear cells. The paper appears to be a further edition with a coloured plate of the results published by him before (see this *Bulletin* No. 1, p. 9).

C. M. W.

TROPICAL SORE.

LA CAVA (Francesco). (i) **Sulla Leishmaniosi delle Mucose e del Primo Reperto di *Leishmania Tropica* Flagellata nel Corpo Umano.** [On Leishmaniasis of the Mucosa and the First Discovery of the Flagellate Form of *Leishmania tropica* in Man.]—*Malaria e Malat. d. Paesi Caldi.* 1912. Nov. Vol. 3. No. 11. pp. 310-313.

(ii) **De la Leishmaniose des Muqueuses et de la Première Decouverte de la *Leishmania tropica* Flagellée dans le Corps Humain.**—*Bull. Soc. Path. Exot.* 1912. Dec. Vol. 5. No. 10. pp. 808-812.

The first case of oriental sore in Italy was described by GABBI about three years ago. Since then many cases have been discovered. These have all shown the usual features of the disease. The author now brings forward two cases which show involvement of the mucous membranes of the nose and mouth and resemble in this way the form of the disease described by SPLENDORE, CARINI and others from South America. In one case (a man aged 40 from Bovalino) there was an ulcerating papule on the mucous surface of each angle of the upper lip. *Leishmania tropica* was found in these. In the second case a slight excoriation about the orifice of the right nostril was noticed. It was covered by a scab

and bled readily. Extension into the nasal cavity took place and a framboesial-like condition of the septum resulted. Inside the mouth the hard and soft palate showed whitish or brownish spots, which suggested that there had been lesions resembling those of the nose, but which had already healed. The right nostril was much reduced in size by the growths and consequently there was some difficulty in nasal breathing, while the voice was changed. The patient, a woman twenty years of age, suffered from anaemia and its effects and occasional febrile attacks. Leishmania were discovered in the nasal lesions. [The author considers these cases to be analogous to those described by Splendore and Carini from South America. It must, however, be admitted that the South American cases with the extensive involvement of the nasal and buccal cavities offer a different picture to the two cases here described, with the small papules on the inner surface of the lip and the growth about the nasal orifice. The author has not shown that the markings in the mouth were connected with the disease.]

The author states that he has found beside the typical leishmania other elongate forms like those described by Splendore (see this *Bulletin* No. 1, p. 12). He further claims to have found, though much more rarely, elongate flagellate forms similar to those met with in cultures. This discovery he made over a year ago but did not feel justified in recording an observation of this importance on a single case. More flagellate forms have been found in the cases which form the subject of these papers so that the author now records his observation with confidence. Apparently these flagellate forms were found within the cells.

C. M. W.

Laveran (A.). **Présentation de Macaques Inoculés avec Succès au Moyen d'une Culture de la *Leishmania* du Bouton de Delhi.**—*Bull. Soc. Path. Exot.* 1912. Oct. Vol. 5. No. 8. pp. 573-575.

The cultures used for the inoculations were obtained from Row in India and were from a Cambay sore. Two monkeys, a *Macacus sinicus* and a *Macacus cynomolgus*, were inoculated with success. The best results were obtained by inoculating in the skin as in vaccination against small pox. One monkey developed sores on the frontal region and external surface of the thigh, and they were still developing after a period of 74 days. The other monkey similarly had three sores on the frontal region, and one on the thigh. Some of the sores were in the form of unulcerated papules, while others were ulcers covered by scabs. Leishmania were constantly present in the lesions.

The author points out that his results resemble closely those obtained by Nicolle with North African sore, so that he regards the Indian and African diseases as identical.

A dog and several mice proved refractory to inoculations with the cultures.

C. M. W.

v. Petersen (O.). **Die Salvarsanbehandlung der Orientbeule (Leishmaniose).** [The Treatment of Oriental Sore by Salvarsan.] —*München. Med. Wochenschr.* 1912. Nov. 12. Vol. 59. No. 46. pp. 2491-2496.

The author points out that Borovsky first described the Protozoa from oriental sore in 1908, from cases of the disease in Tashkent, but that the publication was made in a Russian military journal and did not attract the attention of the outside world. The author has made a tour through south-east Russia, visiting the following places—Tashkent, Buchara, Aschabad, Kokand. In all, 120 cases of oriental sore were seen and these shared 364 sores between them. The cases conformed to the usual type of the disease. Details are given of the parts of the body infected and the ages of the individuals. Treatment was carried out on 36 cases by intravenous injections of salvarsan. There were 31 favourable results (sixteen cured, four nearly cured, and eleven much improved). Two appeared to be unaffected by the drug while the three remaining cases were not heard of after treatment. The drug was dissolved in distilled water and given in a dose of 0·4-0·6 gram for an adult. Of fifteen cases completely cured healing took place in fourteen days in six cases, in six days in three cases, in eight days in two cases, and in ten, eleven, nineteen and thirty days in four cases.

The author concludes that salvarsan in these doses is a specific against the Protozoa causing oriental sore and advises the use of this drug in its treatment on account of its rapid action. The dose may be repeated in a couple of weeks if improvement is delayed. It is likely to be of much use in the case of those in military service, where it is undesirable that long invaliding from duty should be caused by the disease.

C. M. W.

Erratum.

Bulletin No. 1 (November 15, 1912), p. 14, third line from end of first paragraph. For the words "Over three weeks" read "Over three months."

MALARIA.

Epidemiology.

Christophers (S. R.). **Malaria in the Andamans.**—*Scient. Memoirs by Officers of the Med. & San. Depts. Govt. India.* 1912. New Series No. 56. 48 pp. With 1 plate and 1 map. Calcutta: Superintendent Government Printing, India.

In this memoir the author gives an excellent account of malaria as it occurs in the Andaman Islands. Altogether fifteen tables are given which illustrate many interesting points, *e.g.*, spleen rate among children and adults, in the various villages. The observations recorded enable some very definite conclusions to be drawn regarding the disease in these parts.

The chief carrier in the Settlement is *Nyssomyzomyia ludlowi*, a species which breeds in and about salt swamps, and was not found at a greater distance from salt or brackish water than half a mile. The species of parasite proved to be carried by this anopheline was malignant tertian. It is probable as happens with other species that it carries all forms of the parasite. The author is doubtful whether any part is taken in the transmission of malaria by the other common species *Nsm. rossi*, and *Myzorhynchus barbirostris*.

Owing to the distribution of *Nsm. ludlowi*, malaria in the settlement is confined to a belt around the margin of the harbour, and is absent or nearly so from villages more than half a mile from the sea coast or the salt swamps associated with this. This freedom from malaria is seen even in inland villages situated on the margin of swamps, amidst rice fields and near jungle.

The endemicity even within the malaria belt is not strikingly high and only one large village (Port Mouat) showed a spleen rate of over 50 per cent. This moderate endemicity is associated with a moderate prevalence only of anopheles.

Suitable conditions for breeding of anopheles were unlimited, but fish of the genus *Haplochilus* were very common and were found in all waters except those of a very temporary nature.

The predominating type of parasite among the children in the villages was simple tertian. Among convicts admitted to hospital and among the convalescent gang quartan infection formed 50 per cent. or over. The carrier was the same, and there is little reason to doubt that the quartan parasite predominated in the case of the labouring convicts, because circumstances favoured relapses whilst actual transmission of the disease was not very active.

It is interesting to note that though infection with malignant tertian at the time of the author's visit was very little in evidence yet the only two infected anopheles encountered were infected with this type of parasite.

There is some reason to believe that proportionate prevalence of the different forms of parasites in any community is dependent upon:

(1) Activity of transmission (numbers of Anopheles carriers).
(2) Factors increasing or diminishing the number and continuance of relapses.

Malignant tertian (producing gametes) most abundantly increases whenever transmission is active, *i.e.*, the number of anopheles are high. Quartan, producing few gametes, but peculiarly prone to relapse and to remain for long periods in the blood, relatively increases when transmission is low but factors favouring relapses high. Simple tertian is an intermediate form, able to assert itself most when transmission is moderate and the antagonism to relapses not too high (native children as against well fed Europeans who suffer most from malignant tertian due to fresh infection).

It remains to be seen whether the frequency of relapses at different periods after the original infection does not differ in the case of different parasites, still further enabling us to explain the prevalence of different species under any given conditions.

The author summarises his conclusions regarding malaria among the labouring convicts. He thinks that the chronic ill health in them is due to relapses, and not as a rule to re-infection.

In conclusion certain recommendations are given regarding the prevention of malaria amongst the self supporters and free population; also amongst the labouring convicts.

In regard to the free population, a malarious village ought to be moved either at once or gradually to a malaria-free site. In the case of convicts it is advised, in some cases, to change the site of the barracks. Antimosquito campaigns might be introduced by filling up swamps close to important stations. Quinine prophylaxis is recommended.

J. G. Thomson.

Rossi (Giacomo). **Sull Rapporti fra Malaria ed Agricoltura.** [Malaria and its Relationship to Agriculture.]—*Atti d Società Italiana per il progresso delle Scienze.* IV. Riunione. Abstracted in *Policlinico.* Sez. pratica. 1912. Dec. 15. Vol. 19. No. 51. pp. 1880-1881.

The author thinks that the study of malaria and its relationship to agriculture is most incomplete. It is pointed out that malaria decreases in most cases where there is advanced cultivation of the soil. In North Italy, where cultivation is less owing to the climate and where there is an abundance of permanent irrigation, it takes a longer time to get the place healthy than in the South where cultivation is more advanced.

J. G. T.

Cultivation.

Thomson (John Gordon) & McLellan (S. W.), with a Note by Sir Ronald Ross. **The Cultivation of one Generation of Malarial Parasites** (*Plasmodium falciparum*) **in Vitro, by Bass's Method.**—*Ann. Trop. Med. & Parasit.* 1912. Dec. 30. Vol. 6. No. 4. pp. 449-459. With 2 plates.

Thomson and McLellan, working in the Royal Southern Hospital, Liverpool, have successfully grown the malarial parasite in vitro, from two patients infected with *Plasmodium falciparum.* The technique used was practically identical with that described by Bass, the only points of difference being a slight increase in the amount of dextrose employed relative to the

quantity of blood. The authors, for example, used 1/10 cc. of a 50 per cent. solution of dextrose to 8 cc. of blood drawn and incubated at 38° C., while Bass used 1/10 cc. of dextrose to 10 cc. of blood and incubated at a temperature of 40° C.

The cultures were examined at intervals of twelve hours, twenty-five hours, twenty-seven hours and thirty-two hours. Smears were made in the ordinary way and stained with Giemsa or modified Romanowsky solution.

The authors describe the morphology of the parasites as seen in the culture tubes. Before inoculation the plasmodia varied in size, with a maximum diameter of about 3μ; they also varied in shape though the ring forms predominated. After twelve hours incubation, at a temperature of 38° C., a very definite increase in the size of the parasites was to be noted and these now had a maximum diameter of 5μ to 6μ. A round mass of pigment about 1μ in diameter was observed, usually situated at one pole of the parasite. The chromatin was situated in the centre, and seemed to have increased in quantity. After twenty-five hours incubation a most remarkable appearance was noted in fixed specimens prepared from two culture tubes, definite segmenting forms being seen in large numbers, showing the nucleus broken up into definite masses of chromatin, which varied from two to thirty in number. The diameter of these schizonts varied according to the amount of segmentation that had taken place, the maximum being about 7 to 8μ. The pigment mass was quite distinct and where segmentation was nearly completed the merozoites were concentrically arranged around it, thus forming the so-called "rosette."

A coloured plate is given showing the parasites before inoculation and after twelve and twenty-five hours incubation. A plate of microphotographs is added showing these characters. A noticeable feature in the cultures was the tendency of the parasites to clump together.

The authors cultivated parasites from two different patients. Several culture tubes were prepared from each. In those prepared from the second patient segmentation did not proceed so far; that is, the number of merozoites was less.

This diversity of number is capable of various explanations:—

(1) That there are two or three varieties of the malignant parasites.

(2) At the time the observations were made segmentation may have been more or less complete.

(3) The administration of quinine in the case of the second patient may have in some way lowered or modified the vitality of the parasite and thus prevented complete segmentation.

Thomson and McLellan are proceeding with these experiments with a view to elucidating several points of interest. Sir Ronald Ross adds a note to the paper; he is quite convinced that there is indisputable evidence that *Plasmodium falciparum* has been successfully cultivated up to the sporulation forms.

The authors did not succeed in cultivating a second generation.

H. B. Fantham.

OLPP (Dr.). **Die Reinkultur von Malariaplasmodien nach Bass und Johns.** [Cultivation of Malaria Plasmodia by Bass and Johns' Method.]—*Münch. Med. Wochenschr.* 1912. Nov 26. Vol. 59. No. 48. pp. 2623-2625.

A description of the work of BASS and JOHNS (see this *Bulletin*, No. 1, pp. 22-24).

J. G. T.

SYMPTOMATOLOGY.

DAGORN & HEYMANN. **Douleurs Néuralgiques Paludéennes des Extrémités.**—*Bull. Soc. Méd. Chir. de l'Indochine.* 1912. Nov. Vol. 3. No. 9. pp. 588-593.

GRALL has pointed out that malaria may be responsible for causing certain nervous affections, *e.g.*, orbital neuralgia, facial neuralgia, intercostal neuralgia, headaches, or localised fever. These conditions are to be explained by a localised action, either of the parasites or of the toxins, on the cerebro-spinal system and the peripheral nerves.

The authors describe the case of a soldier who was seized with peculiar neuralgic pains in his extremities, burning sensation in the feet, with a slight degree of asphyxia of the extremities like that described by RAYNAUD.

The patient, aged 26, gave a history of specific disease which was treated with mercury and "606" injection. During a march he was seized with acute pains in his feet; there was no rise in temperature. After admission to hospital several very severe attacks of pain in the feet occurred and these extended as far up as the knees; at the same time pains in the hands and forearm as far as the elbows were complained of. During these crises the temperature was elevated from 38·8° C. to 39·9° C. and the patient was unable to refrain from crying out. He received injections of hermophenyl and "606." No quinine was administered. The patient rejoined his regiment, but returned to the hospital a second time with a note to the effect that he was suffering from syphilis and nervous troubles, with extremely painful crises in the arms and legs. The temperature at the time of second admission was 40° C. During the attacks of pain the temperature was elevated; there was slight oedema of the feet, and the knee jerks were absent. The blood showed malignant tertian parasites.

The authors at first hesitated in giving a definite diagnosis. The history of syphilis and the existence of malaria made it doubtful whether the crisis was due to his previous attack of specific disease or was caused by malaria. Specific disease was excluded because no benefit was derived from mercurial treatment, and two injections of "606" were given without effect. A diagnosis of neuralgic pains due to malaria was made, owing to the crisis occurring with the attacks of fever and the presence of malignant tertian parasites in the blood. All symptoms disappeared with rigorous quinine treatment and the patient was discharged in a perfect state of health, with his knee jerks present.

J. G. T.

ZUCCARELLI. **Paludisme Aigu; Complications Méningitiques; Signe de Kernig.**—*Bull. Soc. Path. Exot.* 1912. Nov. Vol. 5. No. 9. pp. 713-715.

Malaria is endemic on the east coast of Corsica between Bastia and Solenzara. The author describes a case of malarial fever in a young boy, aged 8, living in this district. The patient had had no previous illnesses and all his family were healthy. He evidently contracted malaria at Alistro railway station where anophelines were numerous. When seen by a doctor the boy was very ill; vomiting was very frequent, and the patient complained of headache; his temperature was elevated. KERNIG'S sign and stiffness of the neck, with a continuous cry, enabled a diagnosis of meningitis to be made. The patient turned with difficulty in bed and the least effort caused sickness.

The author considers this to be a case of malaria showing signs of meningitis. The patient was given chlorhydrate of quinine 0·20 cgm. and pyramidon 0·05 cgm. every 6 hours; on the third day there was no fever; on the fourth day there was no headache. The pyramidon was stopped and 0·25 cgm. of quinine was given morning and evening. After a week of treatment the child refused quinine and the temperature again became elevated. Treatment was renewed, continued for a month, and a complete cure resulted.

[The author does not state whether he found parasites in the blood.]

J. G. T.

TREATMENT.

CESTAN (R.) & PUJOL (M.). **Paludisme et Arsenobenzol.**—*Gaz. des Hôpitaux Civ. et Milit.* 1912. Nov. 12. Vol. 85. No. 129. pp. 1793-1796. With 2 curves.

The authors draw attention to the fact that arsenic has long been used in the treatment of malaria. This drug has two therapeutic actions, a tonic and a parasitic. Since the introduction of "606" for the treatment of syphilis, the possibility of its use in the destruction of the malarial parasite has become a matter of much interest, especially in those cases which are resistant to quinine. The observations of WERNER, NICOLLE, CONSEIL, IVERSON and TUCHINSKY show that the efficacy of salvarsan depends on the particular type of malaria. The benign tertian parasite disappears altogether after an injection, but the parasite of the malignant type, although it disappears after treatment, tends to recur. In short, treatment by salvarsan cures the benign tertian, but does not prevent the recurrence of malignant tertian malaria.

The authors give a description of two cases of malaria which were treated with salvarsan, and they publish the temperature charts. [The type of malaria is not indicated but probably it was benign tertian.]

They point out that the injection of "606" should be given at the beginning of the attack of fever, when the young forms predominate. In the two cases reported a rapid recovery was obtained in both after a single intravenous injection.

An interesting observation is made regarding the Wassermann reaction in malaria. Böhm, Jaworski, Boermann and Wetter found a positive Wassermann in 20 to 40 per cent. of malarial cases. This has been disputed by Blasi and Tschiknawaroff. The authors point out that in their two cases a positive Wassermann was converted into a negative one by treatment with "606."

J. G. T.

Fusco (Vincenzo). **Il "606" nella Infezione Malarica.** [Salvarsan in Malaria.]—*Gazz. d. Ospedali e. d. Cliniche.* 1912. Nov. 14. Vol. 33. No. 137. pp. 1433-1434.

The author made observations on three cases of aestivo-autumnal malaria. Salvarsan in doses of 30 centigrammes was given in each case. The conclusion is that the aestivo-autumnal parasite is not destroyed by this drug, but nevertheless in one case it was useful in preventing relapses.

J. G. T.

Rosati (Beniamino). **La Splenectomia nella Malaria cronica con Cachessia in rapporto alla Emolisi Splenica.** [The Operation of Splenectomy for Chronic Malaria with Cachexia.]—*Gazz. Internaz. Med. Chir. Igiene.* 1912. Dec. 14. No. 50. pp. 1186-1193; and Dec. 21. No. 51. pp. 1205-1215.

The author gives a full description of three cases of chronic malaria with cachexia and enlarged spleen, in all of which the operation of splenectomy was performed. The first two gave a satisfactory result, but in the third death occurred; this was due to the serious condition of the patient who had great enlargement of the spleen. In all the cases profound anaemia and wasting, which were uninfluenced by medical treatment, were also present.

The blood changes before operation were as follows:—leucopenia, diminution of the red cells, diminished haemoglobin, poikilocytosis, with increase in the mononuclear leucocytes and blood platelets. In the third case there was no diminution in the leucocytes and the polymorphonuclears were in excess.

In the first two patients, who survived the operation, the blood examination after splenectomy revealed the following:—continued increase in the red blood cells as well as haemoglobin; a transient increase in the leucocytes, especially the polymorphonuclears.

The character of the blood in the two successful cases showed hyperactivity of the lymphatic glands in spite of the fact that these were not enlarged. The bone marrow, however, judging by the blood picture, showed little activity. In case 2 a month after the operation relapse of fever of an undoubted malarial character occurred accompanied by enlargement of the liver.

The results obtained in an investigation of the haemolytic properties of the serum can be given as follows: (*a*) The serum of the splenic vein gave excessive haemolysis of healthy red blood corpuscles, as well as those from the peripheral blood of the patient, and also those from the splenic vein itself. (*b*) The

serum of the peripheral blood of the patients gave only a medium haemolysis of healthy red blood corpuscles, and those from the splenic vein, but had no action on the patients' own corpuscles in the peripheral circulation. This haemolytic power of the peripheral blood disappeared after operation.

In conclusion, the author says that the results obtained demonstrate that splenectomy represents the radical cure of chronic malaria with cachexia, since the spleen in this affection is not only seriously changed but has become an organ dangerous to life, acquiring the haemolytic properties which the author has demonstrated.

J. G. T.

PROPHYLAXIS.

LEGENDRE (J.). **Sur la Destruction des Moustiques à l'Aide du Filet.**—*Presse Méd.* 1912. Aug. 14. Vol. 20. No. 66. (Chronique.) p. 854.

The author describes a modified butterfly net which he advocates as a useful instrument for the capture and destruction of mosquitoes and flies. The gauze pocket is conical in shape and deep, and tapers to a point, instead of being rounded like the ordinary butterfly net. This modification prevents captured mosquitoes from escaping during the chase of others. With this net the author states that as many as 50,000 to 80,000 mosquitoes have been captured during a day in one establishment. He suggests that in the hands of young children it would provide a useful amusement.

J. G. T.

CARTER (Henry R.). **Antimalarial Measures for Farmhouses and Plantations.**—*U.S. Public Health Reps.* 1912. Dec. 6. Vol. 27. No. 49. pp. 2024-2030.

Malaria is essentially a rural disease; it is found in towns only as they approach rural conditions—that is, in small towns and in the suburbs of large cities—not in the bodies of large cities. For this reason antimalarial measures applicable to farmhouses and plantations are of interest. Carter fully discusses the subject of prevention under two headings (1) The measures involving the control of the human host. (2) Measures involving the control of the insect host.

He summarises his conclusions as follows:—

For farm houses antimalarial measures based on the control of both the human and the insect host should be used.

Of the first, the isolation of men sick of malarial fever from mosquitoes is the most important.

Of the second, draining mosquito breeding land near the house, especially to windward, is of great value.

Of almost equal value is the screening of the house. This is always possible. Drainage unfortunately is not always possible in many parts of the country. Until drainage is done screening must be our sheet anchor in preventing malarial fever in farmhouses.

The problem of drainage should be taken up both by the individual farmer and by the community, just as plantations and country roads are.

J. G. T.

GABBI (U.). **Malattie Infettive. Malaria.**—*Commissione Govern. p. l. Studio d. Malattie Tropicali nella Libia. Malattie Infettive e Malattie cutanée.* 1°. *Contributo ad opera di U. Gabbi, F. Scordo, G. Rizzuti.* (Ministerio d. Intern. ed. Guerra; Direz. Gen. d. Sanità Pubblica.) 1912. Messina; Stab. Tipograf. Guerriera. pp. 13-16.

Gabbi discusses tropical diseases in Cyrenaica and Tripoli. The use of quinine is unknown in some of the provinces, especially amongst the poor population of Tripoli; a service was established by which quinine was distributed free. Fifty-six patients were treated for malaria; of these 51 showed the malignant tertian type of fever, 3 were quotidian and 2 quartan. The attack of fever occurred about noon in all the 51 malignant tertian cases. With regard to the prevention of malaria Gabbi advocates the following precautions:—

(1) Keep the concentration camps of Arabs a good distance from Tripoli. (2) Use quinine prophylaxis in these camps—by giving quinine twice a week or every other day. (3) Give notice to Europeans that in choice of domestic servants they should not neglect to obtain a certificate from a medical man, certifying that they are free from chronic malaria.

J. G. T.

MISCELLANEOUS.

Southern Medical Journal. 1912. Aug. Vol. 5. No. 7. pp. 439-459.

This number contains the following original articles:—

(i) WHITE (J. H.). **The Eradication of Malaria.** pp. 439-444. (ii) JACKSON (T. W.). **A Malarial Hot Bed within sight of National Capital.** pp. 444-449. (iii) HENSON (Graham E.). **A Review of the Possible Aetiological Factors in Malarial Recurrence; the Significance of such Cases and their Treatment.** pp. 450-457. (iv) BOOTH (B. H.). **Pernicious Malaria with Cerebral Symptoms resembling Heat-stroke, with Report of Cases.** pp. 458-459.

(i) White discusses the problem of malarial prevention. The actual work of eradication of malaria is elemental in its simplicity, but calls for untiring watchfulness and absolute thoroughness. The author thinks that the increase of the population in the Northern and Middle States of America has practically obliterated malaria without any interference on the part of the physician, because the land owing to its value has been drained. In many parts of America, however, this condition does not exist, and so palliative measures have to be employed. Where thorough drainage is impossible exclude mosquitoes from houses by screening, drain small pools of water near at hand, oil those which cannot be drained, and never forget that gamete-carrying patients must be given quinine. It is advocated that the interest of the nation and the state ought to be aroused, and big swamps might thus be obliterated. The drainage of the huge swamps in the south would clear out malaria and yellow fever and render that part of America as healthy as Northern Europe.

(ii) Jackson discusses the presence of malaria at Fort Washington in a military reservation which is within sight of the Washington monument. A chart is given showing the monthly incidence of malaria cases for five years. The author says that quinine prophylaxis was a failure at Fort Washington. A campaign was begun against mosquitoes, and the population protected from bites. [This paper is to be continued.]

(iii) Henson gives a very full resumé of the causes of recurrences in malaria. The author thinks that parthenogenesis cannot be considered a factor in recurrence for the following reasons:—

(1) The very existence of such a phenomenon is a matter of great doubt, many observers working over a period of years having failed to demonstrate such forms. (2) There are many cases reported that have at no time during the infection shown the sexual forms, but have frequently relapsed. (3) Four cases are cited by Ross in which inoculation experiments of blood containing only sexual forms failed in each instance to produce clinical symptoms of malaria, while in fifty-one cases cited by the same author, inoculation experiments of blood containing asexual parasites in every instance produced clinical symptoms of the infection.

The author says that asexual reproduction by schizogony is generally accepted as the cause of short interval relapses, but the length of time that the schizont is capable of keeping the infection alive in man without producing clinical symptoms is at present undetermined. The observations of Craig that certain forms of the plasmodia exist only when conjugation is present and often before gametes have appeared would indicate that they are a factor in recurrences of long intervals.

(iv) Booth draws attention to the fact that comatose malaria may be wrongly diagnosed as heat-stroke. In pernicious malaria the first indication of the attack is the development of acute delirium or sudden and deep coma. The temperature may be high or sub-normal. The pupils are contracted, usually pin point in character, and fail to react to light. The tongue is coated, usually having a whitish fur on it. The odour of the breath is sweetish. The respirations are shallow and vary from 20 to 50 per minute. All secretions are diminished and the pulse varies from 120 to 150 per minute. These symptoms simulate very closely those of heat-stroke. Four cases of comatose malaria are described; all made a good recovery after antimalarial treatment.

A discussion followed. Von Ezdorf adhered to the parthenogenetic theory as the cause of relapses. Schaudinn, he said, believed in it and reported having observed it. McElroy saw no evidence from a study of the blood that conjugating forms developed in the body, but on the other hand he thought that parthenogenesis was a well established principle. Henson in closing the discussion thought that the thick film method of Ross was very useful in diagnosis, and advocated the treatment of patients for two to four weeks with 30 grains of quinine daily. The disagreeable symptoms caused by the quinine disappear very largely after a week's treatment.

J. G. T.

SIMPSON (G. C.) & EDIE (E. S.). **On Haemoglobin Metabolism in Malarial Fever. Part ii. The Influence of Quinine.**—*Ann. Trop. Med. & Parasit.* 1912. Dec. 30. Vol. 6. No. 4. pp. 443-447.

In a previous paper it was shown that the amount of haemolysis proceeding in the body can be measured to some extent by the total excretion of urobilin. In malaria a high degree of haemolysis is followed by a high excretion of urobilin in the faeces, and sometimes also in the urine. In another paper (see this *Bulletin* No. 1, p. 21) it was shown that a haemolytic principle occasionally can be demonstrated in malarial serum; this action is most likely to be shown by the serum of a benign tertian case drawn at the onset of a paroxysm.

Simpson and Edie now contribute a further paper on their researches carried out in the Liverpool School of Tropical Medicine. Their conclusions are as follows:—

(1) Increased excretion of urobilin may occur after the administration of quinine in doses of ten to thirty grains a day. A similar result follows injection of blood pigment or haemolytic drugs.

(2) Quinine probably possesses the power of determining haemolysis in the body, though the exact mechanism of its action must be further investigated.

(3) Individual or pathological idiosyncrasy may exaggerate this action and so account for the influence of quinine in blackwater fever.

J. G. T.

O'CONNELL (Matthew D.). **The Meteorology of Malaria.**—*Jl. Trop. Med. & Hyg.* 1912. Aug. 15. Vol. 15. No. 16. pp. 245-246; and Nov. 15. No. 22. p. 340.

The first paper deals with Allahabad. Here the night atmosphere in September, when malaria is prevalent, is compared with that in the humid cotton weaving sheds of Lancashire. The temperature at Allahabad is nearly as high and the humidity is much greater. Hence exposure to the night atmosphere at this town in September must raise the body temperature more than exposure to the atmosphere in the cotton sheds. The author regrets that malariologists never discuss the effect of exposure to the night atmosphere on body temperature. They mention meteorological conditions only in the briefest manner, and then merely point out their effect on mosquitoes and their larvae, or on the extra-corporeal phase of the malarial parasites, the oocysts of which are said to develop best at 68° F. to 86° F., and are killed by temperatures below 60·8° F. During the height of the malaria season in Allahabad (September) the night temperature ranged from 77·3° F. to 84·7° F. dry bulb, with a relative humidity per cent. of 93·0 to 74·0.

In the second paper the author gives, through the kindness of the Deputy Director of the Madras Observatory, hourly observations of the dry and wet bulb temperatures, and the velocity of the atmosphere at Madras from 6 p.m. on September 21 to 6 a.m. on September 22, and from 6 p.m. on September 22 to 6 a.m. on September 23 1912; that is, for two nights in what is known as the unhealthy season in India.

Tables are given shewing a comparison between the atmospheric conditions in Madras and those of the cotton sheds in Lancashire. The inference is that immersion in the September night atmosphere at Madras must produce pyrexia in a considerable number of the inhabitants.

J. G. T.

ADIE (Helen A.). **Note on the Sex of Mosquito Larvae.**—*Ann. Trop. Med. & Parasit.* 1912. Dec. 30. Vol. 6. No. 4. pp. 463-464. With 1 plate.

The dark or brown testis can be distinguished in living anopheline larvae by a lens; or, if the larva is very young, say about three days old, by a two-thirds lens. Often the testes are more easily seen from the ventral surface. In the female larva the ovary lies in about the same situation as the testis in the male, but stretches through two or three segments owing to its length. Figures are given showing the position of the testes, which are situated at the 6th abdominal segment. Other figures show some of the more minute structure of the sexual organs.

J. G. T.

RELAPSING FEVER.

Transmission.

Deutz. **Über Versuche zur Übertragung von Hühnerspirochäten auf Mäuse.** [Experiments to Infect Mice with the Fowl Spirochaete.]—*Hygienische Rundschau.* 1912. Aug. 15. Vol. 22. No. 16. pp. 1017-1019.

By means of intravenous and intraperitoneal injections of 0·5 cc. of the blood of a fowl heavily infected with spirochaetes, the author was able to infect mice with *S. gallinarum.* After an intravenous injection the parasites could still be found in the blood of the mouse 72 hours later, whilst, after an intraperitoneal injection all disappeared within 24-48 hours, phagocytosis taking place more rapidly in the peritoneal cavity than in the blood. By means of intravenous injections the fowl spirochaete could be transmitted from mouse to mouse for only two passages, but by the employment of intraperitoneal injections into very young mice (ten to twenty days old) three passages were obtained. A mouse which has once been infected with this parasite cannot be reinfected and its serum contains certain substances (immobilisins) which at once arrest all motion of the spirochaetes. Thus, when the serum of a recovered mouse is mixed with blood containing fowl spirochaetes, the latter are quickly immobilised and subsequently devoured by the phagocytes, whereas normal mouse serum has no effect on the parasites. When the spirochaetes are disappearing from the circulation of a mouse the number of blood platelets increases enormously.

In conclusion, the virulence of a strain of fowl spirochaetosis is considerably diminished by passage through a mouse, the incubation period in fowls being lengthened from 48 hours to more than six days.

E. Hindle.

Cultivation.

Noguchi (Hideyo). **Cultivation of** *Spirochaeta gallinarum.*—*Jl. Experimental Med.* 1912. Nov. 1. Vol. 16. No. 5. pp. 620-628. With 1 plate.

Employing the same culture media and methods as those used in the cultivation of other spirochaetes (see this *Bulletin*, No. 1, p. 40) the author has succeeded in cultivating *Spirochaeta gallinarum* for many successive generations. The most suitable fresh tissue to employ was found to be a piece of either the pectoral muscle of a fowl, or rabbit's kidney, and a certain amount of oxygen seems to be necessary, for in vacuo the spirochaetes were unable to grow.

The maximum growth is reached about the fifth day, after which degeneration slowly commences, and the parasites usually disappear entirely within 15-21 days from the inoculation of the culture. In one case, however, living spirochaetes were observed in a culture thirty days old, that had been kept at 37° C. the whole time. The spirochaetes still remained virulent for chickens after having passed through at least thirteen sub-cultures, but at

times individual cultures under certain conditions suddenly lost their virulence. The inoculation of such cultures into fowls produced no infection, but rendered the birds refractory to subsequent inoculation with a virulent strain.

The author adds some remarks on the morphology of the parasite as observed in cultures. Those grown in media containing rabbit kidney instead of chicken muscle are somewhat thicker than usual but otherwise are normal in behaviour. The author has never seen longitudinal division in this species; unmistakable examples of tranverse division preceded by strangulation (= incurvation) have been observed, thus confirming HINDLE'S account of the division of the *S. gallinarum*. The many small round or oval granules that appear in old cultures are considered to be degeneration products, as the author was unable to cause their development into spirochaetes either in cultures or by inoculation into chickens. The larger round bodies, 0·75μ in diameter, formed either at one end or along the length of the spirochaete are considered to represent a stage in the life-cycle, and not plasmolysis as described by HINDLE. The author states that at no period of cultivation did any bacillary forms appear, such as those present in the tick.

Several filter experiments were performed to ascertain whether cultures of *S. gallinarum* contain any form which passes through a Berkefeld filter (V), but no infection was ever produced by the inoculation of the filtrate into chickens. Moreover the filtrate did not contain any form that could be grown in culture media. Similar results were obtained in the case of cultures of *S. duttoni*, *kochi* (= *rossi*), *obermeieri* (= *recurrentis*), and *novyi*, respectively.

E. H.

SYMPTOMATOLOGY.

CASAUX (J.). **Considérations Cliniques sur la Fièvre Récurrente en Indochine.**—*Rev. de Méd. et d'Hyg. Trop.* 1912. Vol. 9. No. 2. pp. 97-118.

After a brief summary of the history of relapsing fever in various parts of the world, in the course of which the author mentions that this disease was first recorded in Indochina in 1907, Casaux proceeds to a description of the clinical features of the malady in Indochina.

Five distinct types are recognised:—

(1) The Ambulatory Form, which is so benign that the patient is almost unaware of its presence. It is characterised by the presence of spirochaetes in the blood unattended by any pathological symptoms, with the possible exception of slight fever.

(2) The Ordinary Form, characterised by attacks of moderate severity, without diarrhoea, constipation, or severe febrile symptoms. The patient may present one, two, or even three attacks, after which recovery is complete.

(3) The Typho-Bilious Form, first recognised by GRIESSINGER in Egypt. This type of relapsing fever is characterised by the occurrence of rather severe febrile attacks accompanied by bilious

vomiting and diarrhoea. The spleen and liver are much enlarged and there is excessive muscular hyperaesthesia. A noteworthy feature is the marked epistaxis towards the end of each attack; the temperature falls as low as 34·2° C. before returning to the normal. This form not infrequently causes the death of the patient, usually during the first febrile period or the interval between it and the relapse.

(4) The Typhoid-like Form, distinguished by its resemblance to typhoid. There is abundant yellow, serous diarrhoea; the stools are sometimes mixed with blood. The temperature is irregular without any marked intervals between the febrile attacks.

(5) The Bilious Form, is distinguished by the occurrence of marked jaundice commencing suddenly on the first or second day of the attack. The liver is very painful both on pressure and percussion. Usually this form is associated with constipation and the stools are not discoloured, but occasionally, on the contrary, there is a bilious diarrhoea.

In addition the author gives some useful summaries of the frequency with which the various symptoms appear. Out of 161 cases, 44 suffered from only one febrile attack; 55 showed two attacks; 37, three; 19, four; 3, five; and 3, six attacks. The average duration of the first attack was six days; the interval between this and the second attack, eight days; duration of the second attack, four days; second interval, seven days; third attack, three days.

In conclusion the author advocates the use of intravenous injections of 0·2-0·3 gms. salvarsan in the treatment of this disease in China.

E. H.

Browse (G. V.). **A Special Type of Recurrent Fever due to a Spirochaeta.**—*Indian Med. Gaz.* 1912. Oct. Vol. 47. No. 10. pp. 387-390.

This paper contains an account of a distinct type of relapsing fever occurring at Quetta, a hill town on the frontier of Baluchistan. The disease is shewn to be due to a spirochaete, morphogically identical with *S. duttoni* and *S. recurrentis*. The clinical symptoms, however, differ from those of recurrent fever, especially in the mild nature of the disease and the distinctive type of pyrexia with many paroxysms of short duration. There is a poorly marked polymorphonuclear leucocytosis with a well marked relatively large mononuclear increase. In the latter features it differs from European relapsing fever, but resembles it in some of the clinical features. It resembles the relapsing fever of Tropical Africa, but develops under such very different climatic conditions that it is regarded as distinct. In one year eighteen cases were observed, most of them amongst the regimental followers who lived in dark huts adjoining the barracks. In spite of their proximity the disease did not occur amongst the soldiers living in the barracks.

The clinical features are described as follows:—

"The onset was sudden with a feeling of cold but no actual rigor. Vomiting was the exception and in no case was jaundice or rash noticed. All the patients invariably felt perfectly well directly the fever ceased and much resented being detained in hospital. A few, after late relapses became anaemic and debilitated, otherwise the disease was trivial in its effects. Pains in the limbs and joints were not uncommon, but were only marked in three cases out of the eighteen. Eight patients had enlargement of the spleen on admission, but of these, five were men with chronic splenitis not due to the spirochaetae. Pain and tenderness over the spleen and liver during the fever paroxysms was observed in three cases, but was the exception."

The temperature follows a course resembling that of African relapsing fever and it is also interesting to note that, as in the case of this latter disease, foreigners are more liable to infection than the natives. Out of sixteen cases the number of febrile paroxysms in each was as follows:—

Number of paroxysms ...	1	2	3	4	5	6	7
,, cases	2	3	3	2	2	3	1

The paroxysms usually lasted from 48 to 64 hours at the commencement of the disease and gradually diminished in length and intensity.

In addition the author discusses the possible mode of transmission of the infection. *Cimex* and *Pediculus* are put out of count because, from their large numbers, there ought to have been many more cases of the fever if these animals had been responsible for the transmission. In the same buildings where the disease occurred, considerable numbers of *Ornithodorus tholozani* and one example of *Argas persicus* were found. One experiment was made with the former of these parasites, ticks which had fed on an infected patient being allowed to feed on a healthy person, but the result was negative. The author considers it improbable that *O. tholozani* carries the disease, because from its voracious habits more of the people inhabiting the building would have been likely to become infected. He suggests that if *A. persicus* were the carrier, it would explain the rarity of the disease, for this tick only exceptionally bites man. The question arises whether the disease is the same as miana occurring in Persia and said to be conveyed by *Argas persicus*.

The description of this interesting Quetta spirochaetal fever is accompanied by charts and tables illustrating the clinical features of the disease.

E. H.

JUKES (A. M.). **Preliminary Note on Some Cases of Spirillar Fever in the Darjeeling District.**—*Indian Med. Gaz.* 1912. Dec. Vol. 47. No. 12. pp. 476-477.

The author describes the presence of small localised epidemics of fever in the Darjeeling district, the diagnosis of which has presented some difficulty. In particular, an epidemic of fourteen cases is described which occurred in one small isolated group of houses, amongst the Gurkha Tea Garden coolies. The patients fell ill in batches of two or three at a time, with intervals of about three weeks separating the batches. All the patients presented the same symptoms, *i.e.* fever, usually about 101° to

102° F., but in some cases going up to 104° to 105° F.; headache; jaundice with varying intensity; nausea, but no vomiting; there was no albuminuria. The first eight patients became delirious, comatose and died about the seventh or eighth day of the disease. The next three recovered but were still weak when seen by the author and the last three were still ill and had had fever for about six days. These last three patients eventually recovered.

Spirochaetes (one to six per field) were found in the blood of one of these patients, but the examination of the other two was negative. There is little doubt, however, that all these fourteen cases had suffered from the same disease.

Since this epidemic the author has observed spirochaetes in the blood of three other patients from different localities in Darjeeling, and in every case the symptoms were the same as those described above. Two were middle-aged men who both recovered after being very seriously ill for some days; the third was a pregnant girl of 20, who miscarried and afterwards died on the ninth day of the disease. All these patients stated that others members of their families had suffered from the same disease, and in several cases death had resulted. Blood from these three patients was examined daily and in every case there was a diminution in the number of spirochaetes after about the sixth day, together with a simultaneous rise in the number of polymorphonuclear leucocytes. This was very marked in the case of the girl who died, who had a high leucocytosis and an absence of parasites the day before her death. In the other two patients the spirochaetes disappeared about the eighth or ninth day.

The author regards this as a new form of "spirillar fever" for the following reasons:—

"1. The severity of the illness and the high mortality accompanying it.

"2. The duration of the fever 8 to 10 days.

"3. The absence of relapses in those who recover."

In addition the author inclines to think that the spirochaete is shorter, thinner and less motile than *S. recurrentis*, but no stress is laid on this point. Attempts to keep the spirochaete alive, either in culture media, or by inoculation into white rats, were unsuccessful.

[The extreme severity of these cases of relapsing fever is very remarkable, and combined with the absence of relapses and the long duration of the fever, the Darjeeling relapsing fever may represent a distinct variety. It should be remembered, however, that under adverse conditions the mortality from relapsing fever may be very high, for Dutton and Todd* mention one case in which, out of twenty carriers in one caravan who contracted the relapsing fever of Tropical Africa, no less than ten died.]

E. H.

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* Dutton and Todd (1905). The Nature of Human Tick-fever in the Eastern Part of the Congo Free State. *Liverpool School of Tropical Medicine. Memoir* XVII. p. 3.

Treatment.

Launoy (L.) & Levaditi (C.). **Nouvelles Recherches sur la Thérapeutique Mercurielle des Spirilloses (Sp. des Poules et Syphilis du Lapin).**—*Compt. Rend. Soc. Biol.* 1913. Jan. 10. Vol. 74. No. 1. pp. 18-21.

The authors have continued their researches on the therapeutic action of organic mercury compounds* and in the present article discuss the action of a new group of products, the dinitro and diamino derivatives of the mercury salt of paradioxydiphenyl. The only one that was found to be of any practical use was the diacetyl derivative of the mercury salt of dioxydiaminodiphenyl. For convenience, this compound is referred to as No. 114. It contains 42·8 per cent. of mercury and is employed in alkaline solution, prepared as follows:—0·2 gms. No. 114 + 2 cc. N/-NaOH + 18 cc. of 9 in 1000, NaCl solution.

Employing the intravenous mode of injection, the toxic dose for the rabbit was found to be 0·04 to 0·05 gms. per kilo., and for the fowl 0·05 gms. per kilo. (of body weight). The authors tested the effect of the compound on *Spirochaeta gallinarum* in fowls. One fowl, that received an injection of 0·04 gms. per kilo. twenty-four hours after being inoculated with the disease, was cured. Two others were injected with equal quantities of the drug, one at the time of inoculating the spirochaete, and the other when the parasites were numerous in the circulation. Neither was cured and the second fowl died as a result of its diminished resistance to the toxic effect of the compound.

The authors also give the results of treating five rabbits experimentally infected with syphilis in the scrotum. Three of the rabbits were cured, but large doses had to be employed (0·03 to 0·04 gm. per kilo.), and in two of them a second injection was required. In one case, however, a single dose of 0·035 gms. per kilo. completely cured a rabbit in twelve days.

Although this compound possesses such a feeble toxicity, the curative dose approaches so closely to the toxic one that in all the animals cured a marked diminution of the body weight was observed as a result of the injection. This diminution, however, was only temporary and the animals quickly recovered their loss in weight.

E. H.

Castelli (G.). **Ueber Neosalvarsan.**—*Zeits. f. Chemotherapie.* 1. Teil. Orig. 1912. Vol. 1. No. 2. pp. 122-135.

The author has studied the action of neosalvarsan in vitro on *Spirochaeta gallinarum*, *S. recurrentis* and *Trypanosoma brucei* respectively. After contact with the drug for periods of fifteen to sixty minutes all these parasites were still actively motile, but had lost their vitality; for when injected into animals they produced no infection. In order to eliminate the introduction

* Launoy & Levaditi. *Compt. Rend. Soc. Biol.* 1912. April 27. Vol. 72. p. 653.

of any of the drugs together with the parasites, the mixtures of neosalvarsan and parasites were centrifuged, by which means the latter were separated from the solution. Solutions of atoxyl had not this parasiticidal action in vitro, the parasites maintaining their virulence. These results shew that there is a direct combination of neosalvarsan with the chemoreceptors of the parasites. This combination seems to occur only in those arsenical compounds containing trivalent arsenic.

The author comes to the following conclusions respecting the action of organic arsenical compounds on parasites. First, the most important factor is the direct combination of the drug with the chemoreceptors of the parasite, quickly arresting its development; secondly, other combinations of the medicament with the body cells of the host, resulting in the formation of substances which directly kill the parasites; and thirdly, it is not impossible that the parasiticidal action of these compounds is supplemented by the action of the body cells of the host.

[It is to be regretted that this interesting paper should contain a number of wrong reference numbers in the text, making it somewhat difficult to look up the literature to which the author refers.]

E. H.

CASTELLI (G.). **Ueber Neosalvarsan. Bestimmung der Toxizität und der heilenden Wirkung bei experimentellen Spirochätenkrankheiten.** [Neosalvarsan. A Determination of its Toxicity and Curative Action on Spirochaetal Infections.]—*Zeitschr. f. Chemotherapie.* I. Teil. Orig. 1912. Vol. 1. No. 3. pp. 321-351. With 1 plate.

The author compares the toxicity of neosalvarsan with that of salvarsan in mice, rabbits, fowls, and pigeons, respectively. Both subcutaneous and intravenous injections were employed and the results clearly show that whereas neosalvarsan is much less toxic than salvarsan when administered intravenously, when the drugs are injected subcutaneously salvarsan is less toxic than neosalvarsan. The author's results are summarised in the following table which gives the *Dosis tolerata* of the two drugs in the above-mentioned animals, employing the two methods of injection.

Animal.	Method of Injection.	*Dosis Tolerata* Salvarsan	Neosalvarsan
Mouse (per 15 gms.) ...	Intravenous	0·002145 gm.	0·00375 gm.
	Subcutaneous	0·00375 „	0·001275 „
Fowl (per kilo.) ...	Intravenous	0·08 „	0·06 „
	Subcutaneous	0·25 „	0·1 „
Pigeon „ ...	Intravenous	0·08 „	0·12 „
	Subcutaneous	0·09 „	0·04 „
Rabbit „ ...	Intravenous	0·1 „	0·2 „
	Subcutaneous	0·15 „	0·1 „

When neosalvarsan is injected either subcutaneously or intramuscularly it is more rapidly oxidised in the tissues than

salvarsan, and in consequence is more toxic. It is evident, therefore, that the intravenous method is the only one suitable in the use of neosalvarsan.

The second part of the paper contains an account of the action of neosalvarsan on infections respectively of *Spirochaeta recurrentis* in mice, fowl spirochaetosis, and syphilis in rabbits. Mice infected with a virulent strain of relapsing fever were cured only on the first day of infection by a subcutaneous injection of 1 cc. of a $\frac{1}{400}$ solution of neosalvarsan (per 20 gms.), whereas the subcutaneous injection of an equal amount of salvarsan invariably cured the mice even at the height of the infection. When the drugs were administered intravenously, a 20 gm. mouse on the first day of infection required a dose of 1 cc. of $\frac{1}{300}$ solution of neosalvarsan in order to be sterilised, whilst a dose of 1 cc. of $\frac{1}{500}$ salvarsan is sufficient to produce the same curative effect. In comparing the values of the two compounds, however, their toxicities should also be taken into account and then one finds that neosalvarsan is two and a half times as effective as salvarsan. With fowl spirochaetosis the author obtained exactly similar results.

The rabbits employed were infected with syphilis by means of subcutaneous injections into the testicles. The strain of syphilis was very virulent and all the rabbits injected developed typical chancres on the scrotum. The animals were then injected with solutions of either salvarsan or neosalvarsan and the results compared. The action of both compounds was very marked, the chancres usually being completely cured within an average of about 26 days; the healing of the sores is well illustrated by a series of photographs. A comparison of the curative doses respectively of the two compounds shews that neosalvarsan is at least twice as effective as salvarsan in the treatment of syphilis in rabbits.

Finally the author summarises the advantages of neosalvarsan as follows:—Its great solubility and the neutrality of the solution. Moreover its curative action on rabbit syphilis is twice as great as that of salvarsan and in other spirochaetal infections the difference in the curative action is equally well shewn.

Although only through clinical experience can one know what will be the effect of neosalvarsan on human spirochaetal infections, the above described data certainly indicate that the new compound is likely to be even more useful than its forerunner, salvarsan.

E. H.

MESSERSCHMIDT (Th.). **Die chemotherapeutische Beeinflussung der Hühnerspirochätenkrankheit, durch die im Handel befindlichen Jodpräparate.** [The Chemotherapeutical Action of some Commercial Iodine Preparations on Fowl Spirochaetosis.]—*Zeitschr. f. Immunitätsforchung.* 1. Teil. Orig. 1912. Nov. 2. Vol. 15. Nos. 2 & 3. pp. 293-302.

Employing fowls infected with *Spirochaeta gallinarum* as indicators, the author has tested the effects of a number of commercial iodine preparations on spirochaetes. The only one

which was found to have any action was the sodium salt of sozoiodol (= Na salt of di-iodo-para-phenol sulphonic acid). This compound merely had a preventive action when injected into the fowls daily from the time they were inoculated with the parasites. Under these conditions the fowls merely shewed a slight infection and soon recovered, whereas all the controls died. On the other hand, once the spirochaetes were present in considerable numbers in the blood the injection of the compound had no effect. It is evident, therefore, that iodine compounds are of very little use in the treatment of fowl spirochaetosis.

E. H.

MOUNEYRAT & TANON. **De l'Action de Nouveaux Dérivés Arsenico-sulfurés dans les Trypanosomiases et les Spirilloses expérimentales.**—*Rev. de Med. et d'Hyg. Trop.* 1912. Vol. 9. No. 2. pp. 139-146.

The present article calls attention to the fact that MOUNEYRAT and not EHRLICH was the first to suggest the use of neosalvarsan in the treatment of syphilis. The paper contains an account of the chemical constitution and derivation of various arsenical organic compounds. In conclusion the authors mention some inconclusive results obtained in the treatment of infections of *S. duttoni* and *Trypanosoma gambiense* by one of these substances (the monomethylene sulphonate derivative of salvarsan).

E. H.

KOCH (W. V. M.). **Relapsing Fever and its Treatment by Salvarsan.**—*Far Eastern Association of Tropical Medicine: Trans. Second Biennial Congress held at Hong Kong.* 1912. pp. 272-277.

The author gives an account of the treatment of two patients suffering from relapsing fever, a disease which is rarely seen in Hongkong, though common in North China, and some parts of South China. The patients were injected intravenously with respectively 0·5 and 0·6 gms. of salvarsan. In both cases the parasites disappeared from the circulation within six hours and the patients rapidly recovered. In its action it seems to imitate a natural recovery; there being the preliminary fall in the temperature, the rigor, and then the sudden drop to the normal together with the disappearance of the parasites from the blood.

A table is given shewing differential leucocyte counts of cases of relapsing fever and primary and secondary syphilis respectively. These were made every six hours after injection of salvarsan and the results shew that leucocytosis is much more marked in the case of relapsing fever than primary syphilis. There was no marked variation in the case of secondary syphilis.

Two of the cases of relapsing fever came from one house and the author considers it probable that either bugs or lice must have been carriers.

E. H.

Classification.

Dobell (Clifford). **Researches on the Spirochaets and related Organisms.**—*Arch. f. Protistenkunde.* 1912. Vol. 26. pp. 119-240. With 5 plates.

Although in the present paper the author has studied non-parasitic spirochaetes only, his results are of great importance from a general point of view, as they conclusively shew the bacterial affinities of this group. After a description of a number of new species of spirochaetes belonging to three different genera, and also some closely related organisms, the structure and life-histories of the spirochaetes are discussed in an analysis, which also includes a review of previous work on the subject. There is no antero-posterior differentiation in the group, each extremity being alternately anterior and posterior, a character which is characteristic of most plants and not of the Flagellates. In addition the body is flexible and capable of plasmolysis, but there is a gradation in these characters from the comparatively rigid and non-plasmolysable *Bacillus flexilis*, through *Paraspirillum vejdovskii* and *Saprospira* up to the very flexible and easily plasmolysed *Treponema*. In all cases where the organism is sufficiently large to decide the point, the protoplasm of the spirochaetes is found to present a chambered structure. A definite nucleus is absent, the chromatin being distributed in the form of chromidia. Special organs of locomotion are absent. In every case, Dobell has only seen transverse division, sometimes binary and in other case multiple. Longitudinal division has never been observed and the author is convinced that it does not occur in the group. In spite of certain peculiarities this transverse division resembles that of Bacteria and Cyanophyceae. The life-cycle is very simple and comprises neither cyst formation, sexual phenomena nor polymorphism. The transverse dimensions of any particular species are always constant but the length is variable as in Bacteria.

The author recognises four genera—*Spirochaeta*, *Cristispira*, *Treponema* and *Saprospira*,—as constituting a natural group known as the *Spirochaetoidea*. This group is far removed from the Flagellata but presents some affinities with the Cyanophyceae. As it agrees with the Bacteria in every character except the absence of locomotive organs the author considers that the spirochaetoidea should be classified with the Bacteria, being placed next to the Spirilloidea. The classification of the Bacteria which is adopted is as follows:—

Schizophyta	Bacteria	Haplobacteria	Coccoidea Bacilloidea Spirilloidea Spirochaetoidea
	Cyanophyceae	Trichobacteria	

[It should be noted that Dobell employs the term *Treponema* to include a large number of forms, such as the blood spirochaetes, that are usually regarded as belonging to different genera. It is doubtful whether this view of the close affinity of *Treponema* (sensu Schaudinn) with the blood spirochaetes will be adopted by many authors, but it is certainly necessary to distinguish the parasitic forms from the free living spirochaetes to which the

name *Spirochaeta* was first applied. At the present time the terminology of the blood spirochaetes is in such a state of confusion that it is doubtful what generic name should be applied to them. After the large number of misunderstood and frequently erroneous observations that have been published on the morphology and life-histories of Spirochaetes, it is with pleasure that one reads the present paper, which is undoubtedly the most important contribution to our knowledge of these organisms that has hitherto been published. In the present place it is only possible to give the merest outline of the author's conclusions and the paper should be read in its entirety by anyone desirous of a fuller knowledge of the morphology and systematic position of the Spirochaetes. The Schaudinnian belief in the flagellate affinities of these organisms has finally been shewn to be erroneous and it is to be hoped that no subsequent writer will ever attempt to resuscitate such a view.]

HOFFMAN. **Zur Stellung der Spirochäten im System.** [The Systematic Position of Spirochaetes.]—*Centralbl. f. Bakt.* 1. Abt. Orig. 1912. Oct. 29. Vol. 66. No. 7. pp. 520-523.

The author adds a few notes on the morphology of *Spirochaeta* (= *Treponema*) *pallida* as observed in cultures, and produces evidence in support of GROSS' view that the pathogenic spirochaetes belong to the Spironemacea. Evidence of the chambered structure of *S. pallida* is shewn by those degenerating forms that present sharply defined swellings either at the ends or along the length of the body. In addition the breaking up of the spirochaete into numerous spore forms has been observed in preparations of the parasite obtained from cultures. The author has never seen any sign of longitudinal division in this species and believes that it invariably divides transversely into two or sometimes more individuals, in the latter case resembling the division of *Saprospira*. In the cultures it is noticed that the spirochaetes tend to adhere by their extremities, thus producing very long compound forms that move about as if they were single individuals. Here again is evidence of the relation to *Saprospira*, which also forms long chains of individuals. The author was able to find evidence of the existence of a vegetable membrane surrounding the body of the spirochaete.

In conclusion Hoffman points out the importance of the observations of GROSS on the spore formation in spirochaetes, as these spores are probably formed in the blood and other parts of the body of patients suffering from spirochaetal diseases and might easily be overlooked.

[The observations of this author are of considerable interest as they tend to shew that *Treponema pallida* presents the same features of transverse division and spore formation that has been observed in other pathogenic spirochaetes. It should be pointed out, however, that the spore formation in spirochaetes was observed by BALFOUR and others long before GROSS published his observations on the Spironemacea.]

E. H.

MISCELLANEOUS.

MARCHOUX (E.) & COUVY (L.). **Argas et Spirochètes.**—*Bull. Soc. Path. Exot.* 1912. Dec. Vol. 5. No. 10. pp. 796-798

The authors have investigated the nature of the granules (= coccoid bodies) described by many workers as a stage in the life-cycle of spirochaetes. Continuing their previous researches, they state that spirochaetes may be found in the coelomic fluid of *Argas* that have been kept at 15° C. for eleven months. Accordingly the successful inoculation experiments of LEISHMAN, BALFOUR, HINDLE, etc., are explained as the result of the presence of spirochaetes in the tissues. The parasites are extremely fine and cannot be stained with Giemsa, but only with Gentian violet or some equally intense method.

With regard to the granules the authors have found them in *Argas vespertilionis* from Timbuctoo, *Rhipicephalus* (? *Ixodes*) *ricinus* from France, and also in *Loelaps echidninus*. In the two former the granules were found to elongate under the influence of heat in a similar manner to those occurring in *Argas persicus*. The authors then state that as the granules appear to exist in all the Acariens they have no connection with the spirochaetes.

[In spite of these observations it should be remembered that LEISHMAN and HINDLE have both examined other species of ticks without finding any granules in their tissues. *A. vespertilionis* is a parasite of bats and the latter are well known to be subject to infection with spirochaetes, and the probabilities are that this tick is the intermediate host. Moreover *Ixodes ricinus* feeds on a variety of mammals, many of which are subject to spirochaetosis, therefore, it might easily be infected. The evidence which has been brought forward is certainly not sufficient to disprove the spirochaetal nature of the granules and to warrant the statement that they appear to be present in all Acariens.]

E. H.

HARRISON (L. W.). **A Modification of the Burri Method of Demonstrating** *Spirochaeta pallida.*—*Jl. R. Army Med. Corps.* 1912. Dec. Vol. 19. No. 6. p. 749.

The author finds that a more homogeneous field is easily obtained by substituting for Chinese ink a suspension of collargol. The latter is prepared according to the directions of the makers (Chemische Fabrik von Heyden), one part of the powder being mixed with nineteen parts of distilled water. The powder is put into a black bottle and the water poured on it. After standing for a few minutes the bottle is well shaken and again allowed to stand, when after a final shaking the mixture is ready for use. The suspension is used in exactly the same way as if it were Chinese ink, a loopful of the suspected serum and one of collargol being mixed together at one end of a slide and then spread like a blood-film.

The film may be examined with an oil-immersion lens as soon as it is dry; the spirochaetes appear white on a reddish-brown field, which is almost perfectly homogeneous.

In addition attention is called to the necessity of carefully cleaning the surface of any sores before examination, as under dark-ground illumination the author has observed extremely delicate spirochaetes in the secretion obtained from the surface of sores that were non-syphilitic.

E. H.

DE GASPERI (F.). **Présence d'un Spirochète dans le Sang d'un Cobaye.**—*Bull. Soc. Path. Exot.* 1912. Oct. Vol. 5. No. 8. pp. 589-561.

This spirochaete was obtained in glucose-lactose gelatine cultures of the heart blood of a guinea-pig that had been injected subcutaneously with some garden soil mixed in a mortar with water at 85° C., in order to isolate a septic vibrio. The animal died twenty hours later of typical septicaemia and in the cultures of its blood spirochaetes were observed living side by side with the vibrio in the water of condensation.

The length of the parasite varies from 9·6μ to 24μ and the diameter from 0·3 to 0·4μ. The long forms have five, six, or eight undulations. The extremities are distinctly pointed. Division forms were not observed and as the spirochaetes died in the cultures within 48 hours it was not possible to make a further study of them.

The author injected ten other guinea-pigs with garden soil in order to see whether this procedure was responsible for the appearance of spirochaetes in their blood, but in no case were the parasites obtained in cultures made in the same way as the above, though vibrios were developed in each culture. Accordingly the author believes that this spirochaete is a specific parasite of the guinea-pig.

E. H.

HENRY (Herbert). *Spirochaeta pollachii:* **A New Blood-Inhabiting Spirochaete from** *Gadus pollachius*, **the Pollack: With a Note on the Occurrence of Certain Intra-Corpuscular Bodies in the Blood of the Gadidae.**—*Jl. Path. & Bact.* 1912. Oct. Vol. 17. No. 2. pp. 160-164. With 1 plate.

The author describes a new species of parasite found in the blood of *Gadus pollachius* captured in Port Erin Bay. The parasite was only found twice out of 348 fish examined. In addition intra-corpuscular inclusions were found in several of the specimens and the author suggests that these may represent encysted phases of a spirochaete. There are some difficulties, however, with regard to their interpretation for the blood corpuscules of the *Gadidae* frequently present degeneration forms practically identical with the intra-corpuscular bodies. In view of BALFOUR'S work on *S. gallinarum*, the author inclines to the view that they represent a stage in the life-cycle of the spirochaete, for they closely resemble the intra-corpuscular bodies occurring in fowls.

E. H.

Prowazek (S. v.). **Einfluss hämolytischer Stoffe auf Spirochäten (Spironemacea).** [The Effect of Haemolytic Substances on Spirochaetes.]—*Centralbl. f. Bakt.* 1. Abt. Orig. 1912. Oct. 12. Vol. 66. Nos. 5 & 6. pp. 424-426.

The author shews that foul spirochaetes removed from the blood by centrifuging and subsequently washed in saline are completely immobilised by the addition of ten per cent. saponin. A ten per cent. solution of sodium taurocholate and a two per cent. solution of smilacin, respectively, dissolved the spirochaetes completely, whilst bacilli exposed to these solutions for equal lengths of time were apparently unaffected.

E. H.

TYPHUS.

KLODNITZKY (N.). **Beobachtungen über Flecktyphus in Astrachan in den Jahren 1907-09.** [On Typhus in Astrachan in 1907-09.]—*Centralbl. f. Bakt.* 1. Abt. Orig. 1912. Dec. 30. Vol. 67. No. 5. pp. 338-354.

The author commences by giving a history of this disease in Russia and shows how the epidemics usually follow years of famine. During the years 1907 to 1909 large numbers of cases of both typhus and recurrent fever (*Sp. recurrentis*) were observed in the State of Astrachan and in many cases the author was able to study the course of the infection in detail.

The results of NICOLLE, COMTE and CONSEIL, and also RICKETTS and WILDER are confirmed as regards the transmission of the disease by ectoparasites, especially the body-louse; and by the application of suitable prophylactic measures typhus was almost eradicated from the State by the end of 1909.

Detailed clinical notes of a certain number of cases are given, including that of the author himself, who was infected whilst visiting a house containing typhus patients heavily infested with lice. In one case, that of a laboratory assistant, the patient was directly infected whilst assisting at the post mortem of a man dead from typhus. During the post mortem the assistant pricked his middle finger and after an incubation period of twelve days suffered from a typical attack of typhus. In the majority of cases the incubation period was about twelve days. Temperature charts are given of five of the cases, together with detailed clinical notes. It is interesting to note that in many cases of typhus the author observed changes in the nails, resembling those described by FEER in 1905 as occurring after scarlet fever. This consists of the development of a small fold or ridge at the bottom of the nail. As a result of the bacteriological examination of 70 cases the author was once able to isolate a small bacillus that also occurs in the stomachs of bugs that have fed on infected animals. This organism, named *Bacillus violentus*, was found to be agglutinated by the serum, diluted 1 : 2000, of a typhus patient. It was easily cultured on various media and was found to possess the most extraordinary virulence, for mice injected intraperitoneally with 0·000,000,001 cc. invariably died within twenty to thirty hours. Over 200 mice were used for these experiments and there can be no doubt of the pathogenic properties of this bacillus, which was also very fatal to rats, guinea-pigs, and rabbits.

The author does not express the definite view that this bacillus is the cause of typhus, but considering its agglutination by the serum of patients, it is considered worthy of further investigation and, at present, an examination of the complement fixation is in course of progress (see the article by RABINOWITSCH, p. 400).

E. Hindle.

BIRT (C.). **Typhus Fever.**—*Jl. R. Army Med. Corps.* 1912. Nov. Vol. 19. No. 5. pp. 521-529.

This paper consists of a summary of our present knowledge of typhus together with a consideration of the history of past

epidemics, viewed in the light of the discovery of its transmission by means of body-lice. The author shows how, from this point of view, past epidemics can be explained and gives a very interesting historical resumé of the more important outbreaks of typhus.

Attention is called to the work of MOCZUTKOWSKI who was the first to show that the blood of a typhus patient was infective. In 1876 he inoculated himself with the blood of a patient taken on the tenth day of the fever and eighteen days later was prostrated with a severe attack of typhus. This first successful human experiment was not made known till 1900 and seems to have attracted little notice.

In conclusion the author points out that forty years ago MURCHISON indicated the correct prophylactic measures, which are summed up in the destruction of pediculi. A temperature of 160° F. to 175° F. is said to be sufficient to kill lice and their ova.

E. H.

PROPHYLAXIS.

CONSEIL (E.). **Résultats de la Prophylaxie du Typhus Exanthématique à Tunis de 1909 à 1912.**—*Bull. Soc. Path Exot.* 1912. Nov. Vol. 5. No. 9. pp. 744-747.

Since the year 1909 the war against typhus in Tunis has been based upon the knowledge that the disease was mainly, if not entirely, transmitted by the body-louse. In consequence, whenever a case of typhus was discovered in a house, not only were the clothes and bedding of the patient disinfected by passing through an oven, but also those of all the other members of the family. In addition the patient and also any persons that had occupied adjoining rooms to him, were taken to the public baths and all their ectoparasites carefully removed by washing, followed by an application of camphorated ointment. Any room occupied by the patient and also those adjoining it were also sterilized by means of sulphur. No prophylactic measures were taken against the excrement of the patient or the drinking water.

The author gives a table showing the number of cases in Tunis in each of the four years from 1909 to 1912. In 1909 there were 836 cases; in 1910, 148; in 1911, 180; and finally in 1912, only 22 cases. The disease is much more prevalent during the months of March to August than during the winter months.

In addition the author gives particulars of the result of the prophylactic measures in individual buildings which were known to be centres of infection and shows how it has been possible to eradicate the disease. In 1911 and 1912, all the cases remained isolated, showing how effectively the measures adopted prevented any spread of the infection.

[The excellent results obtained in Tunis lead one to hope that before long typhus will disappear from North Africa in the way that it has gone from Europe. In Africa its disappearance is being hastened by the adoption of efficient prophylactic measures based entirely on a knowledge of the mode of transmission of the disease by the louse.]

E. H.

SERUM DIAGNOSIS, &c.

RIZZUTI (G.) & SCORDO (F.). **Ricerche Batteriologiche e Sierodiagnostiche nel Tifo Esantematico.** [Bacteriological and Sero-diagnostic Researches on Typhus.]—*Malaria e Malat. d. Paesi Caldi.* 1912. Dec. Vol. 3. No. 12. pp. 321-331. **Recherches Bactériologiques et Serodiagnostiques à propos du Typhus Exanthématique.**—*Bull. Soc. Path. Exot.* 1912. Dec. Vol. 5. No. 10. pp. 778-779.

During the Italian campaign in Tripoli the authors have had the opportunity of examining some cases of typhus that occurred amongst the soldiers and also the natives of the country. After a short history of the previous work on the causal agent of typhus, they proceed to a description of fourteen cases in which the authors made a careful bacteriological examination of the patients.

Agglutination tests were tried with the following organisms: Eberth's bacillus, Paratyphoid A and B, *Micrococcus melitensis*, but in all cases the serum of the patients gave negative results.

The authors also attempted to culture an organism from the blood taken from patients on the second to the fourteenth day of the fever. Broth and agar were used as culture media, but uniformly negative results were obtained. In individual cases the cerebro-spinal fluid and spleen were also examined without finding any organisms. Accordingly, the authors consider that typhus is caused by an ultra-microscopic parasite and that the various organisms found in the blood by some investigators are probably the result of secondary infections.

E. H.

RABINOWITSCH (Marcus). **Ueber die Komplementbindung bei Flecktyphus durch den Wässrigen Extrakt aus dem Flecktyphuserreger.** [The Fixation of the Complement in Typhus by a Watery Extract of the Typhus Organism.]—*Deut. Med. Wochenschr.* 1912. Oct. 24. Vol. 38. No. 43. pp. 2018-2019.

During an epidemic of typhus in Kieff during the years 1908 and 1909, the author was able to examine the blood of 58 patients and the organs of 30 that died from the disease. In all cases the author was able to find "*Diplobacillus exanthematicus*" in the organs, and also in the blood circulation, both by cultural methods and microscopical examination. A further proof that this organism is the cause of typhus is afforded by agglutination tests and also by the serum reaction. The fixation of the complement by means of a watery extract of cultures of the "*Diplobacillus*" is described in the present article.

As antigen the author employed a watery extract of a 24 hour culture of the organism on glycerine serum. To this antigen was added varying amounts of typhus serum, inactivated by heating to 55° C. The haemolytic system was then added to the mixture and the whole kept for two hours in a thermostat. In this way the blood of twelve patients was examined and the following results obtained:—

Complete fixation of the complement takes place between the sera of patients taken only after the sixth day of the febrile attack, and extracts of the organism after it has been cultured at least one month, but not more than two months. The sera of healthy persons and also patients suffering from other diseases gave negative results. The sera of typhus patients taken at the commencement of the febrile attack and on the second and third days also shewed no fixation of the complement. Similarly the extract of fresh cultures of the organism obtained from the blood eight days previously gave negative results, even with the serum of the patient from whom the culture had been obtained. When large quantities of serum and antigen were employed, slight fixation of the complement was obtained with sera other than that from typhus patients, but was complete only in the case of the latter.

In spite of the strong evidence that Rabinowitsch brings forward in support of his view as to the causative relation of *Diplococcus exanthematicus* to typhus, it should be noted that many authors have entirely failed to find the organism in cases of this disease. Klodnitzky (*see above*, p. 398) in particular, examined the blood of 70 patients without being able to find it and, therefore, for the present, the causative agent of typhus must be regarded as not thoroughly proved.

E. H.

Anderson (John F.) & Goldberger (Joseph). **Natural and Induced Immunity to Typhus Fever.**—*Jl. of Infectious Diseases.* 1912. Nov. Vol. 11. No. 3. pp. 402-410.

After mentioning instances of transient or permanent natural immunity of human beings to certain infections, the authors proceed to discuss the results obtained by them in the inoculation of monkeys with typhus. Working with the New York and the Mexican virus, they found that out of 58 monkeys inoculated with doses of virulent typhus blood, thirteen did not become infected; of these, five did not become infected after a second inoculation, and two failed to react after three inoculations. While recognizing the possibility that in these cases viruses of different virulence may be a considerable factor the authors do not think it probable, as the strain employed had been propagated through 25 monkeys without showing any diminution in virulence. They consider therefore that instances of a transient or permanent natural immunity of the monkey to typhus are not uncommon.

The repeated inoculations of virulent blood, or blood serum, when not followed by a febrile reaction, confer no appreciable resistance. The failure of an animal to react to an immunity test cannot therefore, in the absence of a previous febrile reaction, be interpreted as indicating that it was protected (vaccinated) by the primary, apparently ineffective, inoculation.

In discussing the susceptibility of the monkey, the authors give tables showing the incubation period and length of the disease in a number of monkeys. Ninety-two out of 103 showed an incubation period of six to ten days, and the duration of the illness in

83 out of 102 monkeys was six to eleven days. A typical febrile reaction is always found to confer complete protection against subsequent infection, and the authors mention one case in which this immunity lasted for at least two years. This febrile attack, under experimental conditions, is considered to justify a diagnosis of typhus.

An atypical or poorly defined fever following an inoculation cannot, however, be interpreted as typhus unless it is followed by resistance to subsequent immunity tests,

E. H.

SCORDO (F.). **La Pressione Arteriosa nel Tifo Esantematico.** [Arterial Pressure in Typhus.]—*Malaria e Malat. d. Paesi Caldi.* 1912. Nov. Vol. 3. No. 11. pp. 289-307.

Employing the RIVA-ROCCI method the author has examined the changes in the arterial blood pressure of seven cases of typhus. The results were very inconstant, there being a rise of pressure in four cases and a fall in the remaining three. The author remarks that they seemed to depend mainly on the state of the patient, there being an increase in pressure when the patient was excitable and a decrease when he was unconscious or partly so. In spite of the few experiments it seems unlikely that this field of research will give any useful results in the case of typhus.

E. H.

POROCEPHALIASIS.

SAMBON (Louis W.). **Porocephaliasis in Man.**—*Jl. Trop. Med. & Hyg.* 1912. Nov. 1. Vol. 15. No. 21. pp. 321-327; & Dec. 16. No. 24. pp. 371-374.

Reference is first made by the writer to articles in the *Journal of Tropical Medicine and Hygiene* (Jan. 15, July 15, and September 1, 1910) in which he described the two tongue worms or linguatulids *Porocephalus armillatus* and *Porocephalus moniliformis*, the former belonging to the Ethiopian the latter to the Oriental region. The larval forms of both of these species are known to occur in man within their respective distributional areas and a list of cases recorded in the literature up to date was given. [The adults of these parasites (Fig. A) inhabit the lungs, trachea and nasal cavities of pythons and other snakes, while the larval or nymphal forms, usually found spirally coiled within a cyst, (Fig. B) have been found in the liver, lungs, mesentery and mesenteric glands of man (*Pentastomum constrictum*) and in the same tissues of other animals lions, leopards, monkeys, cats rats and hedgehogs.*]

Fig. A.—*Porocephalus armillatus*, ♀. Natural size.

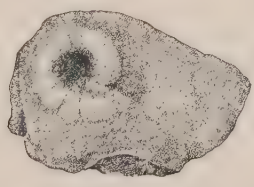

Fig. B.—Nymphal stage of *Porocephalus armillatus* in liver.

In the present paper (i.) the author mentions three more cases ascribed to *P. armillatus* which he did not mention before because they could not possibly have been due to this Ethiopian linguatulid. As two of these occurred in America he believes that the forms found may really have belonged to some species

* Figures A and B are reproduced from a paper by SAMBON in the *Jl. of Trop. Med. & Hyg.* 1910. July 15. p. 213.

of linguatulid inhabiting the Neartic region—to *Porocephalus crotali* for example—so he gives a detailed description of this parasite. The adult forms of *P. crotali* inhabit the lungs of *Crotalus adamanteus, C. horridus, C. terrificus* and other rattlesnakes of the United States. The larval form described by DIESING in 1835 from the marine opossum (*Marmosa murina*) under the name of *Pentastoma subcylindricum* is probably the nymphal stage, but considerable confusion apparently exists between these different forms, at least three different species being confounded with *P. crotali.*

(ii.) In this paper another species of Porocephalus (*P. clavatus*) is described. Its geographical distribution is Central and South America. The adult forms are found in *Boa constrictor* Linn. the common boa and in *Boa imperator* Daud. the emperor boa, while the nymphal forms have been recovered from *Didelphys virginiana* Shaw. the Virginian opossum and in *Philander philander* the philander opossum. At one time the species was confounded with *P. crotali.* Sambon gives amongst other synonyms for it the name of *Pentastomum proboscideum* a form with which an interesting experiment was conducted by STILES (1891). In 1890 STILES in America, found several specimens of *Pentastomum proboscideum* = *Porocephalus clavatus* (according to Sambon) in the lung, trachea and body cavity of a recently imported *Boa constrictor.* He fed a young dog, a guinea pig, a rabbit, a dove and some white mice with the eggs of the linguatulid and got the following results. In the dog (70 days), the guinea pig (82 days), and the rabbit (83 days) after infection, all the larvae were found to have died off at a very early stage of development. Calcification had taken place in the cysts. In the dove no cysts developed as was expected. In the white mice the results were very striking. One of these rodents died 32 days after infection and at the autopsy, on opening the body cavity, Stiles noticed that the liver, kidneys, lungs, peritoneum and even the subcutaneous connective tissues were dotted with numerous spots the size of a pin's head. On closer investigation these spots proved to be the seats of the encysted pentastomes. Contrary to the experience of others no cysts were found in the muscular system. Some of the larvae enclosed by the connective tissue capsule had died at a very early stage of development. This Stiles terms "first stage." Others had attained a condition of development which (according to LEUCKART) is reached by *P. denticulatum* at the end of the eighth week, "second stage." On the forty-fifth day after infection two more mice died. They likewise contained a great number of larvae, all of which had proceeded further in their development than those of the first mouse, "third stage." On June 3, i.e., eighteen weeks and a half after infection, the last mouse was killed, and in it were found a great number of perfectly developed pentastome larvae, some free in the thoracic cavity, others encysted in the various organs, "fourth stage."

These agreed so thoroughly with the description given by LEUCKART of *P. subcylindricum* that STILES now regards as certain LEUCKART'S assumption that *P. subcylindricum* is the

early form of *P. proboscideum*. Later, through LEUCKART's kindness he was able to compare his larvae with a specimen of *P. subcylindricum* found by NATTERER in the liver of a Didelphys (= *Marmosa murina*) in order to establish their identity.

Stiles also endeavoured to infect some European snakes (the common snake, *Tropidonotus natrix* and the common viper *Vipera berus*) by giving them the fully developed larvae from the mice in their food in the hope of obtaining the intermediate stages between the full grown larvae and the adult forms. In both kinds of snakes he recovered the larvae from their body cavity later. In one case they appeared to have grown in size, but in the others, they had either not developed any further, or had died.

G. C. LOW.

LOHLEIN (M.). **Beiträge zur Pathologie der Eingeborenen von Kamerun.** [Summary of the Results of 140 Autopsies in Duala, Cameroons, 1910 & 1911.]—*Beihefte z. Arch. f. Schiffs- u. Trop. Hyg.* 1912. Nov. Vol. 16. No. 9. 110 pp. [Porocephaliasis pp. 58-72.]

The author states that porocephalus larvae are very frequently found in the organs of Cameroon negroes, much more frequently than the literature of the subject would lead one to believe. He refers to SAMBON's paper on 'Porocephaliasis in man' (Jl. Trop. Med. & Hyg. 1910. July 15), in which at that time only about sixteen cases had been recorded in man, in about 70 years, and then narrates how SEIFFERT in 218 autopsies in coloured railway workers in the Cameroons had seen a similar infection seventeen times, i.e., in 7·8 per cent. Löhlein himself found a slightly higher percentage of infections in a series of 118 post mortems on negroes conducted by himself, ten being found with larvae, i.e., slightly over 8 per cent. BRODEN and RODHAIN (quoted from SAMBON) found two cases of porocephalus infection in Congo negroes out of forty post mortems, while of 31 monkeys they found nine (29 per cent.) infected with larvae.

The author follows SAMBON as regards nomenclature of the species and quotes freely from his papers. Anatomical details of the adults and nymphal forms are then given and the exact sites the latter were encountered in are detailed. As regards the effect these parasites produce on the health of the infected human subject opinions seem to vary. 'Most authorities, Löhlein included, seem to think they are harmless but in cases described by CHALMERS, WALDOW and RAEBIGER free wandering parasites were found and in the first observer's case probably were the cause of death. CHALMERS in describing his case stated that 'the presence of the parasite in the human body sets up inflammation of the lungs and the peritoneum, but it does not appear to irritate the alimentary canal or the liver. The disease appears to last some time before causing the death of the patient, for as far as he could determine the Mendi [Sierra Leone Negro] had been ill for a long time.'

In WALDOW'S case, a native, 25 years of age, who died in the Cameroons with symptoms of meningitis, small cysts containing calcified porocephali were found in the liver beneath its peritoneal covering, others in the omentum, mesentery and pleura. In the transverse colon two living and free specimens were found, one within the lumen of the gut, the other attached to the serous covering.

In most cases however the presence of the porocephalus larvae is only detected accidentally at autopsy in cases dying of dysentery, pneumonia, malaria or other diseases. They do not appear to give rise to any special symptoms.

G. C. L.

RAT BITE DISEASE.

HATA (S.). **Salvarsantherapie der Rattenbisskrankheit in Japan.** [Salvarsan Treatment of Rat Bite.]—*Münchener Med. Wochenschr.* 1912. April 16. Vol. 59. No. 16. pp. 854-856.

The author refers to eight cases of rat bite disease treated by salvarsan in Japan. The patients were under the care of TANIGUCHI, KATAYAMA, SAKURANE and other Japanese doctors. Before giving details of these Hata gives a clinical description of the disease and recommends those who wish to study it to read the work of H. MIYAKE (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1899. Vol. 5, No. 2. p. 231). Rat bite disease though common in Japan is little known in Europe. It develops only in a certain proportion of those bitten by rats. The incubation period varies from five weeks to two months, during which time the bite wound usually heals. The invasion is generally sudden with shivering or rigors, weakness, loss of appetite, headache and fever. In most cases the site of the bite now shows inflammatory changes with redness and painful swelling, which may spread to the surrounding tissues producing an oedematous swelling with vesicle formation and even necrosis. A lymphangitis spreading up to the lymphatic glands draining the area on which the bite is situated is also noticeable and later these glands swell and become sensitive to pressure.

The fever, even on the first day of the disease, is high, 39-40° C. and continues so for two or three days. After a profuse perspiration it falls to normal and with the fall the local swelling and inflammation of the lymphatics decrease in intensity.

After some days or after a week another attack of fever, associated with the same symptoms, appears, but is now in addition often associated with a characteristic erythema or a papular exanthem on different parts of the body. Further recurrences are common and the disease generally runs a prolonged course, the temperature often becoming irregular and intermittent. In most cases the tendon reflexes are increased at the commencement of the disease, later they are lost. The liver and spleen are not enlarged. In severe cases there are pains in the muscles and joints, sensory and motor disturbances, oedema of the whole extremity, or even of the whole body, albuminuria, delirium, lethargy and coma. The mortality is about ten per cent. Treatment up to the present time has mostly been symptomatic. Quinine, antipyrin, strychnine, pilocarpine, arsenic and atoxyl are among the drugs that have been tried.

The author then gives a short account of the eight cases treated by salvarsan. In most of those marked improvement followed the injection of the drug, the temperature falling, the inflammation subsiding, the skin eruptions disappearing and the lymphatic glands resolving. In one case the results were not so striking, but still some degree of improvement was noticeable. In two cases

a relapse appeared. In those however the dose had only been 0·3 and 0·4 gram and the author believes that this was not large enough.

G. C. L.

CRUICKSHANK (Robert W.). **A Note on Rat-bite Fever, with Report and Temperature Chart of a Recent Case.**—*Brit. Med. Jl.* 1912. Nov. 23. pp. 1437-1439.

The note describes a case of rat-bite disease (Rattenbisskrankheit (German), Sokòshio (Japanese)) occurring in England. As far as the author knows, the only cases that have been reported in the British Isles are three by HORDER (1909-10) and one in 1895 by MIDDLETON of Glasgow. In America several cases have been noted and FRUGONI has recently reported one from Italy. The author believes that at least two others have been met with in Europe, one in France and one in Spain. MIYAKE's types and description of the disease are quoted. These are—

1. A febrile type with a marked eruption.
2. An afebrile type with nervous symptoms.
3. An abortive type.

MIYAKE states that the feverish phase is accompanied by an eruption of purplish spots. The wound heals during incubation, fever begins abruptly. The site of the bite becomes red and swollen, dropsy may appear and in some instances local gangrene is found. The onset is ushered in with chilliness, headache, marked weakness, fever, and an eruption of dusky coloured purple spots. Pain may be felt in the abdomen and diarrhoea may occur. The pulse is rapid and weak and a feeling of precordial pain and palpitation may be complained of. Delirium may be present. The disease runs a prolonged course and recurrences are common at varying intervals.

Cruickshank's case presented many of the features mentioned above, for example, the patient had a well marked rash and in all had fifteen febrile attacks. The longest period between the acme of attacks was eleven days, the shortest, which proved to be an abortive attack, was five days. The intermediary attacks showed eight, seven and six days' intervals. The disease apparently ceased suddenly with an abortive attack about the fifteenth week; the temperature was recorded for a month longer during which time it remained normal or subnormal. No later rash was noted. Convalescence was very slow, the patient suffering much from headaches. He was not able to get about much for six months after the bite but no distinctive manifestations occurred, though he still occasionally complained of giddiness and headache. Treatment by various drugs was tried, aspirin, phenacetin, quinine, sodium salicylate, sodium sulphocarbolate, etc., but none of these seemed to influence the course of the disease. The two first named were useful when headache was severe; later on tonics containing strychnine caused some improvement and appeared especially to benefit the heart.

G. C. L.

FRUGONI (Cesare). (i) **Intorno al Primo Caso Diagnosticato in Italia di Sokodu (Rattenbisskrankheit).** [First Case of Rat Bite Disease diagnosed in Italy.]—*Rivista Critica di Clinica Medica.* 1911. Vol. 12. No. 50-51.

(ii) **Sokòdu (Rattenbisskrankheit).**—*Berliner Klin. Wochenschr.* 1912. No. 6.

Both papers describe the case of rat-bite disease seen by the author in Florence. This is the one referred to in CRUICKSHANK'S paper (see above). In May 1908 the patient was bitten on the right thumb by a rat, two of the teeth of the rodent breaking off in the wound. The bite healed in three to four days. On the fifteenth day the site of the bite became red, swollen and painful and a small ulcer developed. Chilliness, vomiting, headache and fever then appeared, the temperature continuing high for fifteen days and then gradually sinking. Later, round red spots the size of a hen's egg, came out on the trunk and extremities. Later still an irregular fever set in with glandular swellings and for that the patient was treated in Prof. BANTI'S clinique. In May 1909 a new skin eruption appeared and painful cramps in the calf were complained of. In September 1909 and May 1910 further relapses took place. In October 1910 exopthalmos with severe injection of the vessels and oedema of the conjunctiva was noted. The eyesight was good however and GUAITA found no functional or anatomical alterations of the disc. The patient then entered the medical clinic of Prof. GROCCO in Florence where the author had an opportunity of examining him. A blood count showed an eosinophilia of eight per cent., the faeces showed no ova of parasitic worms and Wasserman's reaction was negative. The pathological research of the blood gave no results. Frugoni describes the skin erythema which is so common an occurrence in rat-bite disease as an erythema exsudativum.

Points of special interest in his case were:—

1. The presence of an eosinophilia and

2. The complication of exopthalmos with acute retrocular cellulitis, the latter, according to the author, being analagous to the subcutaneous cellulitis which is the direct cause of the erythema exsudativum. These symptoms have not apparently been previously described. The patient was treated with atoxyl injections but relapsed again later.

In the part dealing with the historical description of the disease, Frugoni states that OGATA believes he has found a protozoal parasite in the blood, in the ulcers, in the skin eruptions and lymph glands of rat-bite cases. OGATA suggests that this may be a sporozoon belonging to the neosporodia and has called it the *Rattengiftsporozoon.* These researches have not been confirmed.

G. C. L.

SNAKE BITE.

BANNERMAN (W. B.). **An Investigation into the Treatment of Snake-Bite by Permanganate of Potassium.**—*Indian Med. Gaz.* 1912. Oct. Vol. 47. No. 10. pp. 381-382.

The treatment of snake-bite by potassium permanganate was first used by FAYRER in 1869, who found that the drug "did not seem to have any power to avert the lethal action of the poison." BLYTH showed that when mixed *in vitro* with permanganate of potassium cobra venom became innocuous. In 1881 COUNY and LACERDA performed certain experiments, showing that the lethal action of serpent's venom was destroyed when a 1 per cent. solution of the drug was injected into the tissues close to the place of bite. ROGERS reported promising results from experiments on various animals. LAMB on the contrary conducted experiments which were not successful. The present investigation was instituted to obtain evidence as to the efficacy of the treatment *in vivo*.

In the first series of experiments natural conditions of biting were imitated as closely as possible. The test dose was that given by the actual bite of the cobra or daboia. The former, after having bitten, remains attached to its prey for an appreciable time, whilst the latter darts with incredible rapidity, and then releases its victim instantly. It occasionally fails altogether in its strike.

The results were as follows:—

"(1) A dog bitten by a cobra cannot be saved by the local application of powdered potassium permanganate rubbed in after free incision of the bitten place; nor by a similar application of a solution of the powder.

"(2) It may be saved by the immediate subcutaneous injection of 10 cc. of a 5 per cent. solution of the drug; but this solution is so strong as to act as an escharotic.

"(3) If this treatment be delayed for even two minutes, it loses its efficacy.

"(4) A dog bitten under natural conditions by a Russell's viper (Daboia) cannot be saved by the drug, however applied."

In the second series of experiments an attempt was made to inject the drug intravenously. It was found, however, that the intravenous injection of even 40 cc. of a half per cent. solution of potassium permanganate caused death from intravascular clotting; so the method had to be abandoned.

In the third series of experiments, the minimum lethal doses of cobra and daboia venom for dogs having been ascertained, solutions of the venom and the drug were introduced through the same hypodermic needle left in situ, so as to make certain that the poison and antidote came into contact. The results showed that even four times the amount which serves to neutralise cobra venom in a test tube will not with certainty prevent fatal poisoning in an animal which has received 10 minimum lethal doses, and that the same quantitative relations obtained when daboia venom was used. It was also found that crystals of potassium permanganate when rubbed into incisions in a dog's leg, produce extensive ulceration, and that, when combined with the local action of daboia venom, the crystals may even cause necrosis of the small bones.

In the fourth series of experiments the test dose given was less than 10 minimum lethal doses and the results obtained are given in a table.

Bannerman's final conclusions are as follows:—

"The conclusions as to the action of potassium permanganate powder on small doses of cobra venom injected just under the skin appear to be that this treatment is of some little use under these highly artificial conditions. It must be remembered, however, that a snake does not deposit its venom under the skin, but striking as it does with its fangs at right angles to the skin, the poison must usually be placed well below the fascia of the part, and therefore further removed from the applications of a chemical antidote.

"With regard to daboia venom injected just under the skin, the results are very similar to those obtained with the venom of the cobra, *i.e.*, that under such artificial conditions the treatment by free incision and rubbing with powder of potassium permanganate is of some little use. As a practical measure for employment after actual snake-bite it appears to be of no use whatever."

G. C. L.

ROGERS (Leonard). **The Present Position of the Permanganate Treatment of Snake-Bite.**—*Indian Med. Gaz.* 1912. Dec. Vol. 47. No. 12. pp. 467-469.

The author criticises BANNERMAN'S paper (see above) and hopes that the publication of the full report will not be further delayed, as on such an important matter full details of the experiments are necessary to allow its value, in relation to the very different conclusions arrived at by other workers, being estimated. For example, BANNERMAN'S statement that "even four times the amount which serves to neutralise cobra venom in a test tube will not with certainty prevent fatal poisoning in an animal which has received 10 minimal lethal doses, and that the same quantitative relations obtained when *daboia* venom was used," may at first sight appear to those unacquainted with the details of the subject as an argument against the value of potassium permanganate. Rogers on the other hand believes that it affords the strongest evidence in its favour and enters into explanatory details. In his own experiments made in 1903, cats were used and the method was signally successful in those animals. He points out that dogs are very unsuitable for experimenting on because they absorb cobra venom with great rapidity. Whatever deductions are to be drawn from these experiments on animals Rogers is certain that the method applied to the human subject has saved numerous valuable lives and gives a table of authenticated bites by cobras and other snakes, in which out of a total of 21 bitten 20 recovered.

Until a more efficient and practical method of treating snake-bite is discovered, he therefore believes that the permanganate method is the one to adopt.

G. C. L.

MAXWELL (J. Preston). **Snakes and Snakebite in the Fukien Province.**—*China Med. Jl.* 1912. July. Vol. 26. No. 4. pp. 243-245.

Snake bite, according to the author, is of comparatively rare occurrence in the Fukien Province of China, poisonous snakes being few in number. Of the latter the following have been

verified:—*Bungarus candidus, Bungarus fasciatus, Naia tripudians, Lachesis mucrosquamatus, Lachesis gramineus, Ancistrodon acutus.*

A list of non-poisonous snakes is given, fifteen being named.

With regard to the poisonous snakes constitutional symptoms do not always follow their bite, in some instances serious local inflammation only resulting. [This is probably due to a slight bite with the injection of a small amount of venom.]

A fatal case in a man after the bite of a *Lachesis gramineus* (green bamboo snake) is narrated, and also two in children after the bite of a *Lachesis mucrosquamatus*; in both great sloughing of the limb took place. A third child bitten at the same time had its leg amputated in the upper third and recovered.

Probably other poisonous snakes occur in the province. The author thanks Lt. Col. Alcock and Dr. Boulenger for help in the identification of the specimens.

G. C. L.

Fitzsimons (F. W.). **The Snakes of South Africa: Their Venom and the Treatment of Snake Bite.** New Edition. 532 pp. With 1 coloured plate and about 200 text-figures. 1912. London: Longmans, Green & Co. Cape Town and Pretoria: T. Maskew Miller. [12*s.* 6*d.* net.]

An entertaining and instructive work. Written both from the point of view of the scientist and the field naturalist, its pages contain a wealth of material which certainly will prove of value to all students of this branch of zoology. Beyond a few isolated contributions to various journals, the author states in his preface that there is no current literature on the snakes of South Africa, their venom and the treatment of snake bite. His work will certainly now supply this.

The typical venomous snakes of South Africa (illustrated by a coloured plate) he gives as follows:—

1. The Boomslang or Tree Snake (*Dispholidus typus*).
2. The Brown variety of Boomslang or Tree Snake (*Dispholidus typus*).
3. The Puff Adder—Pof Adder (*Bitis arietans*).
4. The Night Adder—Nacht Adder (*Causus rhombeatus*).
5. The Coral Snake—Koraal Slang (*Aspidelaps lubricus*).
6. The Hornsman or Horned Adder (*Bitis cornuta*).
7. The Black and Yellow Snake—Zwart en Geel Zee Slang (*Hydrus platurus*).
8. The Mamba or Tree Cobra, black variety (*Dendraspis angusticeps*).
9. The Mamba or Tree Cobra, green variety (*Dendraspis angusticeps*).
10. The Cape Cobra, yellow variety—Geel Kapell (*Naia flava*).
11. The Ringhals or Spitting Snake—Ringhals Slang (*Sepedon haemachates*).

All these, in addition to harmless non-poisonous snakes, egg eating snakes and others, are carefully described, both as regards their anatomy and general habits. The nomenclature adopted in the volume is according to the catalogue of snakes in the British Museum, compiled by the well known authority G. A. Boulenger.

A systematic list of South African snakes for the use of museum curators and scientific students by the same authority is also given in Chapter XIII and should prove of great value.

In view of the recent pronouncement by BANNERMAN on potassium permanganate in the treatment of snake bite (see above), the author's remarks on this subject are of interest. He refers to the experiments of LAUDER BRUNTON, FAYRER, ROGERS, LAMB, RICHARDS, LACERDA and others. In his own experience Fitzsimons has found that this drug destroys the poisonous properties of the venom of all South African snakes and that of venomous insects. He quotes the instance of a man who was bitten once by a full sized Berg Adder (*Bitis atropos*) and once by a Puff Adder (*Bitis arietans*) in whom ligature of the wound and injection of a solution of permanganate of potash seemed undoubtedly to prevent a fatal result. In further experiments he found that when the drug is rubbed into the free

BRUNTON'S "First Aid" instrument. Actual size.

incisions made over the site of injection of snake venom or the direct bites of venomous snakes, recovery frequently takes place when the higher animals are experimented on. Success is in proportion to the quantity of poison injected, and the time which has elapsed between the application of the remedy and the time of the injection of the venom. If the potash is applied five minutes or more after the injection of the venom, it is unsuccessful and death always occurs. In one instance he mixed 50 times a fatal dose of cobra venom with a little permanganate and injected it without any poisonous effect. Judging from his experiments he concludes that if a person be bitten by a venomous snake and rubs permanganate of potash into the incisions made over the site of the punctures and applies a ligature within five minutes of the infliction of the bite, provided that proper secondary treatment is carried out, he will, in most instances, recover. Three important facts must be remembered however: (1) Permanganate when swallowed has no effect at all upon snake venom which has got into the blood. (2) If injected into a vein after symptoms of poisoning have set in it has no antidotal effect. (3) If injected or rubbed into the tissues at the site of the wound ten or more minutes after the infliction of the bite, it is of little or no use as an antidote.

The author also gives brief instructions for the use of anti-venomous serum some of which are as follows:—

(1) Anti-venene is the serum of horses highly immunized with cobra and viper venoms (*Colubrine* and *Viperine*).

Its curative properties have been tested on animals against these venoms and found to be effective.

(2) In case of either cobra or viper bite when the patient is at hand and before symptons have set in, 25 to 30 c.c. of anti-venene should be injected under the skin into any part of the body where the skin is loose, such as in the region of the flanks. For preference inject into the loose tissues or folds of the abdomen at the sides between the last rib and pelvis.

(3) In a case when a patient is not seen until symptons of poisoning have set in, the same amount of serum should be given by injection direct into a vein.

(4) If serum has been injected under the skin, and if the patient seems to be developing alarming symptons, inject at least 25 c.c. into a vein.

(5) For intravenous injection, a vein of the forearm should be selected for preference. A local subcutaneous swelling appearing during the operation of injection shows that the needle is not in the vein, and a fresh attempt should be made to introduce it.

(6) If there be any albuminous deposits or flocculi in the bottle, the serum should be filtered through the corner of a clean linen pocket-handkerchief or a piece of clean rag into a wine-glass or other convenient receptacle previous to using it. This is not essential if injecting under the skin.

(7) The serum syringe should be perfectly clean. The best plan is to boil it in water to which some borax has been added.

If any weak antiseptic such as boracic acid or permanganate in solution be at hand, wash the site of the proposed injection with it. If no antiseptic is to be had, then rub the spot clean.

(8) An albuminous precipitate in the bottle does not indicate contamination and would be quite harmless if given subcutaneously.

(9) The bottles of serum should be kept in the dark, and in the coolest place in the house. Heat and light are the two chief causes in bringing about a deterioration in the strength of the antitoxic properties of the serum.

(10) When kept in a dark and cool place, the serum loses very little of its antitoxic properties in a year—probably not more than five per cent. even if as much.

(11) Serum injected in excess does no harm. Occasionally what is known as serum sickness (anaphylaxis) supervenes, but this is slight.

The book is handsomely illustrated with many excellent photographs. The obtaining of these must have cost the author much patience and labour.

An illustrated booklet by the same author on "Snake Bite and its Scientific Treatment" has also been received.

G. C. L.

CELL INCLUSIONS.

SCHILLING-TORGAU (V.). **Concerning the Origin and Significance of Leishman's Chrome-Cells in Blackwater Fever (The Basophile Granular Leucocyte of Ehrlich).**—*Jl. Trop. Med. & Hyg.* 1912. Dec. 16. Vol. 15. No. 24. pp. 369-370.

The author first draws attention to the so-called chrome cells described by LEISHMAN and states that THOMSON has recognised these as degenerated mast cells. These basophile-granular leucocytes are rare, hardly ever being found in the normal blood in numbers exceeding 0·5 to 1 per cent. This percentage is raised in leukaemia or polycythaemia and the author has drawn attention to their comparative frequency (up to 3 per cent.) in beriberi. They are also found in the blood of natives and inhabitants of tropical countries. The true form of the basophile leucocyte is seldom observed by the Romanowsky method, this apparently being due to the process of fixing and subsequent treatment. For demonstrating them the new Giemsa-acetone quick staining process is recommended. The technique for this is as follows:—

Giemsa solution and pure acetone are mixed in equal proportions, and 15 drops of the mixture are placed on an air-dried preparation not more than 48 hours old at the bottom of a carefully sterilized Petri dish. After one minute pour 15 cc. of distilled water into the dish, mix, leave for 5 minutes, wash and then dry in the usual manner.

As regards the cell inclusions described in blackwater fever by LEISHMAN, the author inclines to the view held by WENYON that the larger of these are really the remains of normoblastic nuclei, the smaller being the well known plasmosomes of WOLF and FERRATA. The latter bodies, he states, are common in the blood of malarial patients. The immature basophile granules, often referred to as the so-called promyelocytes, the primary stages of the real myelocytes, possess a certain resemblance to the inclusions of the chlamydozoa, especially in their first stages inside the cell. Schilling-Torgau found these cells, where aggravated symptoms of blackwater fever and malaria were present, on several occasions, but in no case did he see any bodies which in his opinion were chlamydozoa.

G. C. L.

CASTELLANI (Aldo). **Note on certain Cell Inclusions.**—*Jl. Trop. Med. & Hyg.* 1912. Dec. 2. Vol. 15. No. 23. pp. 354-358.

In this paper various kinds of cell inclusions derived from different pathological lesions are described. The author divides these up under two headings:—

(1) Those of type A or chlamydozoa-like.
(2) Those of type B.

Those of type A were met with in a case of chronic urethritis of non-gonorrhoeic origin, in the epithelial cells of the conjunctiva, and in the epithelial cells of the oral mucosa.

The cell inclusions of type B were quite different from those described under the term type A or chlamydozoa-like. The author

called attention to them in 1905 in some of his papers on yaws. They are of fairly frequent occurrence and may be found in epithelial cells as well as in leucocytes; they may be (1) in the cytoplasm of the cells, or (2) intranuclear. These inclusions take a blue colour with Giemsa's stain, sometimes of a pale tinge, sometimes of a deep hue. They are round, oval, or pear-shaped, the maximum diameter varying from two to five or six microns; they are occasionally vacuolated and almost constantly present some dots of chromatin. As regards the nature of these inclusions, they are not in the author's opinion parasitic, as they are found in diseases of most different etiological nature, such as yaws, psoriasis, acne vulgaris, lichen ruber, etc. They cannot be confused with Ferrata plasmosomes or Kurloff bodies, the former being metachromatic and the latter staining purple or red, nor with the different bodies recently described by Leishman in blackwater fever and by Low in other diseases. Probably they result from degenerated erythrocytes and although the chromatin granules certainly resemble parasitic granules, nevertheless the fact just mentioned that they have been seen in non-protozoal diseases, such as acne vulgaris, disposes of the parasitic theory.

The author's conclusions are as follows:—

"(1) Inclusions of 'type A or chlamydozoa-like' have been observed by me in epithelial cells of the urethra, of the conjunctiva, and of the oral mucosa. I consider them, with the possible exception of those found in the conjunctival mucosa, as merely products of cellular degeneration.

"(2) Cell inclusions of 'type B,' to which I called attention in 1905, oval or roundish bodies, staining by Giemsa or Leishman pale or deep blue, occasionally vacuolated and generally presenting some chromatin dots, are found in yaws, psoriasis, and many other pathological conditions in the leucocytes and epithelial cells. I do not consider them to be of parasitic nature.

"(3) Oval or roundish free bodies, varying greatly in size, are often seen in films from yaws, psoriasis, and other pathological conditions, staining blue and presenting numerous granules which take the chromatin stain deeply. These bodies are degenerated basophile erythrocytes presenting chromatin dots. These blue, chromatin dotted bodies, or fragments of these bodies, are engulfed by the leucocytes and other phagocytic cells, and most probably appear in these cells as inclusions of type B.

"(4) The true nature of the chromatin dots in the free blue staining bodies (degenerated basophile red cells) is unknown, but I adhere to the opinion that they are not parasitic. They are quite different from the more usual granules found in red blood cells. They take the chromatin stain deeply, and closely resemble, in my opinion, the Jolly's granules, though in contrast to these they are present in large numbers, and are always found in basophile cells."

G. C. L.

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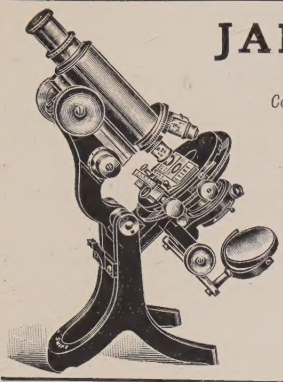

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